Endurance

Notes for mercp-paces

| MRCP-ACES | 2020

To my lovely sweet home MEMSS !

MRCP-PCES

Brief Clinical Consultation

Acanthosis Nigricans

65 years old, complaining of skin rash

Confirmations:

- Self
- Patient
- Agenda

Opening question:

- You got troubled with skin rash, could you tell me more about it?

Brief analysis of complain:

- **Where is the rash exactly?**
- **Can I see it?**
    - There are soft velvety hyperpigmented plaques that are present on the **intertriginous areas** of the **axilla, groin, and posterior neck**
- Any kin rash else where
- **ODPARA**:
    - **Onset**
        - Did it start sudden or gradual?
    - **Duration:**
        - When did it start exactly?
    - **Progression:**
        - Is it increasing, decreasing or the same?
    - **Association:**
        - Any joint pain
        - Any weight changes?
    - **Anything making it better?**
    - **Anything making it worse?**
    - **Any relation to exposure to sun light**
- **Is it painful?**
- **Is it oozing?**

Differential diagnosis of the cause:

- **Obesity**: any weight change?
- **Diabetes**: increase water work?
- **Cushing's syndrome**: skin changes, skin thinning, skin bruises
- **Acromegaly**: hands or feet getting larger, visual disturbances like pumping to objects or not seeing sides of road
- **Thyroid disease**: weather preference, neck swelling

- **Underlying malignancy**: change in bowel habit, high body temperature, pumps and lumps, weight loss

PMH:

- Any medical condition I should be aware of?

FH:

- Family history of similar condition – AD

DH

- Allergies
- Medication list

SH:

- What you do for living?
- How symptoms affecting you in daily life
- Is it distressing to you?
- Smoking
- Alcohol
- Driving – acromegaly
- Female – Private questions – period – PCOS

Can I examine you?

- Start by examining patient concern, the skin rash, axillae, back of neck, intertriginous areas - **hyperpigmented, brown, velvety plaques**
- I would like to examine further to look for possible associations
- BMI: patient looks obese or not
- Facial appearance
- Buffalo hump
- Oral cavity
- Fundoscopy if diabetic plus visual acuity
- Finger pulp for sugar checking marks
- LNS – malignancy
- Organomegaly
- Skin striae and bruises
- Purpura
- Check BP
- Check urine for glucose
- Check blood glucose

What is your concern?

What is wrong with me?

- From what you told me and after examining you, most likely you have a condition called acanthosis nigricans
- Acanthosis nigricans is the name for dry, dark patches of skin that usually appear in the armpits, neck or groin.

- It could be a sign of an underlying condition
- The main symptom of acanthosis nigricans is patches of skin that are darker and thicker than usual.
- They can appear anywhere on the body.
- In rare cases, it can be a sign of something more serious, such as cancer.
- Sometimes acanthosis nigricans happens in healthy people with no other conditions.
- This is more common in people with dark skin.
- We need to do some tests to confirm the underlying cause
- There's no specific treatment for the patches.
- A skin specialist (dermatologist) may be able to suggest treatments to improve their appearance but finding and treating the cause is usually recommended first.
- And will give you appointment to discuss tests results when they are ready
- Is that okay with you?

What is your diagnosis?

- **Acanthosis nigricans**

What are your differential diagnoses?

1. Seborrheic Keratosis
2. Atopic dermatitis
3. Eczema

What are your clinical findings?

How you will investigate this case?

- Basic investigations
- CBC – anemia – GI malignancy
- Blood glucose
- TFT
- Serum cortisol level
- US and CT scan – underlying malignancy
- GI endoscopy

What is the treatment?

1. **Of the underlying cause**
2. **Topical keratolytic medications**- topical tretinoin, salicylic acid
3. **Oral agents** that have shown some benefit include etretinate, isotretinoin, metformin
4. **Cyproheptadine** has been used in cases of malignant acanthosis nigricans because it may inhibit the release of tumor products.
5. **Psoralen plus UVA** (PUVA) has been reported as beneficial for symptomatic relief in cases of paraneoplastic acanthosis nigricans
6. **Laser therapy**

Questions commonly asked by examiners

What are the causes of acanthosis nigricans?

- **Obesity** (most common cause)
- **DM- Insulin resistance**
- **Diabetes**
- **Cushing's syndrome**
- **Acromegaly**
- **Hypothyroidism**
- **Hyperthyroidism**
- **Polycystic ovarian syndrome**
- **Familial** (inherited as an **autosomal dominant** trait)
- **Malignancy** (most commonly an **adenocarcinoma of the gastrointestinal tract**)
- **Drugs** (see below)

What drugs have been reported to cause acanthosis nigricans?

1. Insulin
2. Nicotinic acid
3. Steroids
4. Oral contraceptives
5. Fusidic acid

When acanthosis nigricans is associated with obesity, what happens to skin lesions with weight loss?

- In the context of obesity, acanthosis nigricans is thought to be weight-dependent and the lesions **regress with weight reduction.**

In the presence of internal malignancy, when does acanthosis nigricans appear?

- Remember the rule of thirds:

- **In one third** of cases the skin changes **appear before any signs of cancer** (**up to 5 years**)
- **In one third of cases**, the skin changes **occur simultaneously** with the cancer
- **In one third of cases**, the skin changes occur **after the diagnosis of cancer**
- **Regression** of acanthosis nigricans can **occur with treatment** of the underlying malignancy, and reappearance suggests recurrence or metastases of the primary tumor.

- Acanthosis nigricans is characterized by hyperpigmented, brown, velvety plaques appearing on the skin of the intertriginous areas.
- They often begin as hyperpigmented macules that progress to palpable plaques. They are often symmetrical although a unilateral form is recognized that is inherited as an autosomal dominant trait.
- Often, there are skin tags that are found around the affected areas.
- The **vulva** is most commonly affected in obese females who are **hyperandrogenic** (polycystic ovarian syndrome).
- **Occasionally**, these lesions may occur on the **mucous membranes** of the oropharynx, nose and esophagus.

- In up to **50%** of cases associated with **internal malignancy**
- There is involvement of the oral cavity-the tongue and the lips being most commonly affected **with elongation of the filliform papillae** on the dorsal and lateral surfaces of the tongue and **multiple papillary lesions** on the **commissures of the lips**.
- Oral lesions are often not pigmented.
- Papillomatous lesions may occur on the **eyelids and/or conjunctivae**.
- **Younger patients (<40 years**) are **most likely** to have an **underlying endocrinopathy**, whereas **older patients** (**>40years**) are most likely have an **underlying malignancy**.

MRCP-PACES

BRIEF CLINICAL CONSULTATION

Achondroplasia

You are SHO in rheumatology clinic
Please examine this patient with:
Short limbs
Short stature
Hearing loss
Lower limbs weakness
Lower limb numbness
Knee pain

Confirmations:

- Self
- Patient
- Agenda

Opening question:

- You got troubled with legs weakness, could you tell me more bout it

Empathy and sympathy:

Analysis of the complaints:

- **Analysis of weakness here:**
- **ODPARA**
  - ✓ When did the weakness started?
  - ✓ Where is the weakness exactly?
  - ✓ Is it flobby or stiffy?
  - ✓ Any loss of sensation?
  - ✓ What level?
  - ✓ Any problem controlling water work and back passages?
  - ✓ Any back pain?
  - ✓ Any trauma?
- **Screen for associations when you discover rom appearance that the case is achondroplasia:**
  - **Headache** - hydrocephalus
  - **ICP symptoms** like vomiting, blurring of vision

  OSA

    - **Ear infection** due to compression of acoustic canal
    - **Back pain**
    - **Spinal stenosis**
    - **OA of knee** due to bowing of legs
    - **Numbness in limbs**

Can I examine you?

- Large head
- **Frontal bossing**
- Scar of **VP shunt** in neck
- **? Saddle nose -** midface hypoplasia
- **Normal trunk length**
- **Ask to stand**
- Raise upper limbs and comment on the short limbs compared to trunk
- **Hearing**: recurrent ear infection
- **Back - kyphosis, lordosis**
- Knees – OA
- **Bowing tibia**
- CNS - Lower limbs, power, sensation, reflexes

FH

- AD

PMH

DH

Social:

-
- What do you do for living?
- **QOL**
    - How much symptoms affecting you in daily activity and at work?
- Smoking
- Alcohol
- Any help needed at home like home modification?
- **May I ask you a question, do you have a partner?**
- **Are you planning any future pregnancy?**
- **Your future pregnancy should be planned - mostly need CS**

What is your concern?

What's wrong with me?

- From what you told me and after I examined you, most likely you have a condition called achondroplasia
- It is causes problem in bone growth affecting almost all bones of the body, mainly the limbs, back bone and skull

- Most likely there is narrowing in bone canal in your back affecting the main nerve cable causing the weakness in lower limbs
- This disease unfortunately runs in family
- We need to admit you - limb weakness!
- We need to do some test and scans to confirm diagnosis and to rule out others
- Will give pain killers for your back pain and knee pain
- **Is that okay with you?**

But no one in family having it?

- That's true
- It can result from new mutation in your gene make up

Examiners' questions:

What are your findings?

- Feature consistent with achondroplasia in form of:
    - **Disproportionate short length of limbs compared to trunk**
    - **Bossing of skull**
    - **Depressed nasal bridge**
    - Symmetrical weakness in limb, power grade 3/5
    - Sensation is also affected, in form of light tough and position sense

What is your unifying diagnosis?

- Achondroplasia

What is the lower limbs weakness differential diagnoses?

1. Spinal stenosis
2. Osteoporotic vertebral fracture

What is the achondroplasia differential diagnoses?

- **Hypochondroplasia**
    - Affect conversion of cartilage to bone
    - Mild features
- **Other causes of dwarfism**

How you investigate this case?

- **Diagnosis is mostly clinical**
- Can be confirmed by **genetic test**
- **CT brain** – hydrocephalus
- **MRI**
    - **Craniocervical MRI** findings include **narrowing of the foramen magnum** and **stenosis in the lumbar spine**
- **How you manage this case?**
- **MDT**
    - **Physiotherapist**
    - **Occupational therapist**
    - **Referral to support groups**

        - **Referral to geneticist**
        - **Orthodontic evaluation** should be performed to assess for **dental malocclusion** and **crowding**.
- **Weight management** should be instituted to prevent obesity and its associated comorbidities.
- **Recombinant human growth hormone**
    - r-hGH or HGH therapy should be administered to foster linear growth.
    - Treatment with r-hGH therapy effectively increases the bone growth rate, especially for the first year of use.
    - Initiating therapy at age 1-6 years is recommended to achieve maximum growth benefit.
    - **Long-term studies** to determine final height and randomized, controlled studies to justify prolonged treatment with r-hGH in patients with short stature are **presently not available.**
- **Anti-inflammatory agents, such as nonsteroidal anti-inflammatory drugs (NSAIDs), are useful to decrease pain and inflammation in patients with degenerative joint disease.**
- **Management of complications**:
    - **Ear infection**
    - OSA - Central and obstructive
    - Dental problem - crowded teeth
    - Leg-lengthening surgery
    - Hydrocephalus
- **Anti-inflammatory agents**, such as nonsteroidal anti-inflammatory drugs (NSAIDs), are useful to decrease pain and inflammation in patients with degenerative joint disease.
- **Surgical Options**
    - **Leg-lengthening procedures** using distraction osteogenesis have been performed successfully.
    - These procedures are lengthy, traumatic, and very demanding for both the patient and his or her family.
    - Complications include bone infection, injury to nerves/blood vessels, injury to muscles/tendons, poor bone healing, and unequal lengthening.

What are the causes of short stature?

- **A- Proportionate:**
    - Limbs all short in upper and lower
    - **Face dysmorphic features:**
        - Noonan
        - Down
        - Turner
    - **No dysmorphic features**
        - Familial
        - Endocrine

        - Pseudohypoparathyroidism
        - Cretinism
        - Panhypopituitarism
        - Chronic illnesses
- **B- Disproportionate:**
- **Upper limbs shorter than the lower:**
        - Achondroplasia

What is the cause of achondroplasia?

- Achondroplasia is caused by a mutation in the **fibroblast growth factor receptor 3** (FGFR3) gene
- It is **AD disease**

How you screen for fetal achondroplasia?

✓ **Fetal ultrasonography** is recommended to assist in prenatal diagnosis, if there is concern for achondroplasia

MRCP PACES

Brief clinical consultation

ACROMEGALY

You are SHO in clinic today
Please examine this 53-year-old Mr. Edward who presents with **headaches**
Discuss your findings with the patient and agree a management plan with appropriate follow-up.

Confirmations:

- Self
- Patient
- Agenda

Opening question:

- I got to know you have been troubled with headache
- Could you elucidate more to me about that?

Brief analysis of headache:

- **ODPARA**
  - Course
  - Duration
  - Progression
  - Site
  - Type of pain of headache
  - Timing- more in the morning
  - Grade 0-10
  - Worsening and relieving factors – bending forward, coughing and sneezing
  - Feeling or getting sick
  - Visual disturbance

Systemic review of acromegaly:

- **Head:**
  - Anyone noticed change in your facial features
- **OSA**
  - Daytime somnolence, early morning headaches, snoring
  - **Generalized fatigue**
  - Obstructive sleep apnea (in 50%): due to **macroglossia** or overweight

- **Eye:**
  - Bumping into objects, decreased vision
  - Any change in your visual sight (if you looked straightforward can you see the walls of the room or the sides of the road (bitemporal hemianopia)
  - Ask about progression
  - Any RTA?
- **Husky voice**
  - Thick vocal cords in conjunction with sinus enlargement results in the characteristic deep, resonant voice.
- **Sweating**
- **Neck:**
  - Any skin abnormality in your neck
  - Hyperpigmentation - **skin tags, Acanthosis nigricans**
  - Neck lump (thyroid)
- **CVS:**
  - Chest pain
  - Racing of heart beats
  - Cough
  - SOB
  - CHF: Difficulty of breathing when laying down or with exertion
  - Dyspnea awakening him from sleeping searching for fresh air
  - Leg swelling(cardiomyopathy).
- **GIT:**
  - tummy pain
  - loose motions
  - blood on the stool? (colorectal cancer)
- **Hands**
  - Pins & needles in hands? (carpal tunnel syndrome)
  - Pain: if there is pain do analysis of the pain
    - Type
    - Site
    - Time (more at night)
    - Grade (from 0 – 10)
    - Improving factors – shaking hands
    - Worsening factor
  - Tingling of lateral 3 and half fingers
- **Change in your ring or shoes size - Tight-fitting jewelry**
- **Arms:**
  - Any difficulty of combing your hair or raising up from a chair (proximal myopathy).
  - Exaggerated facial wrinkles
- **Joint pain**

- Any joint pain?
- Where?

- **DM, HTN**
  - DM-increased thirst
  - Drinking more water than you used to?
  - Passing more urine than usual? (diabetes mellitus symptoms, hypercalcemia)
  - Did you check your blood pressure or glucose level – ask about control
- **Check for MEN1symptoms**
  - Werner's syndrome
  - Heart burn (gastrinoma)
  - Dizzy spells, sweating, LOC (insulinoma)
  - Constipation increased thirsty, headache, frequent urination (hypercalcemia of hyperparathyroidism).
  - Passing stones - Urolithiasis (5–10%)

- **Alarm symptoms**
  1. change in bowel habit
  2. rectal bleeding
  3. severe headache with double vision with ptosis (pituitary apoplexy)
  4. Any weakness in your arms or legs?

Drug history

- Check current medications
- any allergies

Past medical history

- High blood pressure
- High blood sugar
- History of cancer
- Any surgeries?

1. Transphenoidal surgery
2. carpal tunnel release

Family history:

- Similar problem or medical disease.

Social history:

- Patient job?
- QOL
  - → if affected say: empasize
  - Refer to a social worker to solve this problem
- With whom the Patient is living?
- Financial support?
- Smoking & alcohol history.

- Can I ask a private question if you allow me?
  - **What about your period? Is it regular?**
    - ❖ Oligomenorrhoea /amenorrhoea, galactorrhoea in females (prolactin is coproduced with growth hormone in approximately 40% of patients with acromegaly)
    - ❖ Loss of lactation
  - **Do you have a partner?**
  - **What about your intimate relationship?**
    - ❖ Impotence in males – loss of libido
- **Driving –** advice you to stop driving ad to inform the DVLA and I will document that in your medical chart

Can I examine you?

- **Start to examine the complaint first:**
  - If visual → start with eye examination
  - If hand pain → start with hand for carpal tunnel
- **EYE**
  - ? Third nerve palsy
  - **Acuity**
    - Counting Fingers
    - Hand Motion
    - Light Perception
  - **Field** - Bi-Temporal Hemianopia
  - **Fundus** - D.M, HTN
    - **Papilledema**
    - **Optic atrophy** due to parasellar extension
- **HEAD**
  - Skin thickening and skinfolds on scalp
- The facial wrinkles may be exaggerated with deepening of forehead and nasolabial creases.
- **'Coarse' facial features**
- **Prominent supraorbital ridges**
- Enlarged nose, lips, tongue and ears
- **prognathism**
  - Prognathism is malocclusion of the teeth where the lower teeth overbite the upper teeth.
  - Ask the patient to clench his teeth and note the malocclusion and splaying of the teeth (i.e. interdental separation)
  - Ask the patient to show his tongue and look for **macroglossia** and for **impressions of the teeth** on the edges of the tongue
  - **Surgical scars**
    1. **Transphenoidal** surgery - inside the nose, around the philtrum and underside of upper lips
    2. **Transcranial** (forehead or side of head)

- **NECK:**
  - **Multiple skin tags** - correlate with the occurrence of colonic polyps
  - **Thyroid swelling**
- **CHEST AND AXILLA**
  - Gynaecomastia
  - Galactorrhea
  - Hyperpigmentation
  - skin tags
  - acanthosis nigricans
  - hirsutism
- **CARDIAC:**
  - Cardiomegaly - hypertension and cardiomyopathy)
  - signs of heart failure → JVP
  - Auscultate bases of lung fields for crepitations
  - Displaced apex suggestive of cardiomegaly.
  - Examine Lower Limbs for pitting edema.
- **SKIN**
  - The skin over the dorsum of the hands is thickened.
  - The skin pores may become noticeably large.
  - Hyperpigmentation occurs in 40% of patients.
  - The nails may become thick and hard.
  - Hypertrichosis or hirsutism (often mild) is seen in up to 50% of patients.
  - Greasy skin
  - Acne
  - Prominent superficial veins of extremities
- **ABDOMEN**
  - **hepatosplenomegaly**
- **HAND:**
  - Spade like
  - Enlarged – doughy
  - Sweating
  - Pulse
  - **Carpal tunnel:**
    - Look for **scars at wrist** for carpal tunnel release surgery
    - **Wasting** of **thenar muscles**
    - Motor **power** for muscles innervated by median nerve.
    - **Sensation** of distribution of median nerve
    - Look for evidence of carpal tunnel syndrome - tap over the flexor retinaculum for **Tinel's sign**
  - **Blood sugar testing marks**
- **KNEES**
  - For OA and chondrocalcinosis Signs
    - Pain & Tenderness

        - Crepitus
        - Painful Limited Range of Movements
- **Back**
        - **kyphosis** - osteoporotic fractures due to hormonal imbalance
- **Proximal myopathy:**
    - **Lower limbs**
        - Ask patient to stand up with arms folded
- **TESTES:**
    - **Large testes**
    - **Small testes** (if hypogonadal)

- Offer PR examination if history indicative.
- Ask to see old photographs?
- Features of hypopituitarism
- Blood pressure for hypertension - present in 15% of cases
- Tell the examiner that you would like to examine the urine for sugar (impaired glucose tolerance).

CONCERNS

What the cause of my headache?

- From what you told me and after I examined you most likely you have a medical condition called acromegaly
- It is due to a growth in a master gland in your head that produces too much of protein called growth hormone affecting different parts of your body leading to your symptoms of change in body appearance, eye symptoms and the pain you have in your hands
- What we need to do is to arrange some blood tests and imaging
- Will refer you to group of specialists including gland doctor, eye doctor for best plan of care and will refer you to social worker

- **For your headaches**, I am going to give **pain killers as a temporary measure** however, it is very important to establish the cause with urgent investigations.
- As your vision is impaired, I am afraid you will have to inform DVLA and stop driving immediately.
- **Are there any further questions or concerns that I can answer for you?**'

What may be the cause for my hands pain doctor?

- The enlargement of the gland I mentioned in your in your head, secreting excessive protein called growth hormone leading to pressure on special nerve in your upper limbs causing the pain in your hands
- We are going to do a special test called nerve conduction study to check that nerve in your upper limbs

What may be the cause for may visual disturbance doctor?

- The same enlargement gland in your head, secreting excessive protein called growth hormone compressing the nerves of your eyes causing your visual disturbance
- I'm sorry you will be banned from driving because it carries risk for you and for public.

Is it treatable condition doctor?

- Yes
- Treatment is available in the form of surgical resection of the enlarged gland (this is the best treatment), or medical treatment (oral tablets) or radiation before the surgery to decrease the bulk of the gland or if you are not fit for surgery
- Your gland doctor will sit with you to explain fully all the available treatment and the best one for your condition

Are those changes in my appearance going to revert?

- Unfortunately, most physical features do not regress after treatment

Why have my hands got bigger and what can be done?

- We need to find out the cause and treat it, with medications and/or surgery.
- Unfortunately, the growth of your hands/feet isn't going to change/ return to normal as these have developed over some time, even years.

Examiners' questions:

How would you investigate this patient?

- **Dynamic GH testing** is via the **oral glucose tolerance test.**
  - **A paradoxical rise in growth hormone** level is **diagnostic** of acromegaly.
  - Failure of GH to suppress to <2nmol/l following OGTT.
  - **Random** growth hormone level measurements are **not useful** because of **pulsatile** secretion.
  - **In patients without acromegaly**, an oral glucose tolerance test **suppresses** GH to **less than 1.0 ng** /ml with in two 2 hours of a 75 g oral glucose load
  - Over 85 % of acromegaly have a value greater than 2.0 ng/mL

- **IGF1**
  - Serum insulin-like growth factor-1(IGF-1) **does not vary diurnally** and is **elevated in virtually all subjects with acromegaly.**
  - It also provides a **measure of disease activity during follow-up.**
  - Allows assessment of the **efficacy of initial therapy** and in the post-therapeutic period
  - IGF 1: used to **monitor disease progression**.

- When IGF-1 levels are only moderately elevated, diagnosis is confirmed by non-suppressibility of growth hormone levels to <1 µg/l after oral administration of 75 g glucose

- **Radiography:**
  - Pituitary fossa (enlarged sella)
  - Sinuses
  - Chest (cardiomegaly)
  - Hand (terminal phalangeal 'tufting')
  - Foot (terminal phalangeal 'tufting', lateral view shows increased thickness of the heel pad)
  - MRI of pituitary
    - Unlike in Cushing's disease and prolactinomas, most of the patients (~60%) with acromegaly have **macroadenomas**.

- **Determine source of excess GH**
  - **MRI of the pituitary detects tumors greater than 2 mm.**
  - Three-quarters are **macroadenomas > 10mm**
  - However, MRI does not determine if the pituitary tumor is functional, and 10-20% of normal subjects will have an incidental pituitary tumor
  - Ectopic GH secretion accounts for only 0.5% of cases.

- **Tests of anterior pituitary function**
  - **Adrenocorticotroph**
    - **short Synacthen test**
    - **insulin tolerance test**
      - In hypopituitarism, the adrenal cortex does not respond sufficiently in the short Synacthen test.
      - It needs to be primed continually by adrenocorticotrophic hormone (ACTH) from a functioning pituitary in order to be responsive.
  - **Thyrotroph:**
    - Check T4 (TSH unhelpful in pituitary disease).
  - **Gonadotroph:**
    - Menstrual history plus estradiol
    - LH
    - FSH
    - Potency plus testosterone - male
  - **lactotroph: prolactin**
    - The prolactin may be low in hypopituitarism.
    - However, production may also be elevated because
      - Some GH-secreting pituitary tumors **co-secrete prolactin**

- **Any pituitary macroadenoma that presses** on the **pituitary stalk** will interfere with dopamine suppression of prolactin production and lead to hyperprolactinaemia

- **Calcium levels**
  - To exclude multiple endocrine neoplasia (MEN) type 1 syndrome
- **Test for complications**
  - fasting blood glucose, HbA1C
  - measure BP
  - Nerve conduction studies for CTS
  - Sleep studies for OSA
  - Formal perimetry
  - Colonoscopy
  - Obtain old photographs
  - Nerve Conductive study For Carpal Tunnel
  - CPK For Myopathy
  - ECG
  - Echo: Dilated Cardiomyopathy
  - Colonoscopy (Above 40 Every 3-5 Years If Active Disease)

Treatment:

What therapeutic options are available?

- The goal of treatment is reduction of symptoms from the local effects of the tumors, increased GH/IGF-I production, or both

Surgical removal

1. **Trans-Sphenoidal Hypophysectomy**
2. **Trans-Nasal Hypophysectomy**
3. **Trans-Labial Hypophysectomy**.

- **First Line of Treatment.**
- **Side Effects:**
  1. Panhypopituitarism
  2. Diabetes insipidus
  3. Hemorrhage
  4. CSF Rhinorrhea
  5. Meningitis
  6. Recurrence

- Remission rates of 80–85% (micro- adenomas) and 50–65% (macroadenomas)
- Diaphoresis and carpal tunnel syndrome often improve within 1 day of surgery.
- Although growth hormone levels fall immediately, insulin-like growth factor levels fall gradually.

Radiotherapy

- For refractory disease or if unfit/unsuitable for operation, or when IGF-1 remains elevated after surgery because of residual tumor
    1. **Stereotactic radiosurgery (gamma-knife)**
    2. **Conventional radiotherapy**
- Decreases GH secretion, but very slowly takes 1–10 years to take effect
- The somatostatin receptor antagonist octreotide is valuable as adjunctive therapy to suppress growth hormone secretion while awaiting radiation.
- Deficiency of other pituitary hormones is common.
- Cranial nerve palsies, loss of vision and memory deficits may also occur

Medical management:

- Pharmacological treatment is used as an adjunct, or where surgery is contraindicated or declined.
- Lead to inhibition of GH release using somatostatin analogues (octreotide) or dopamine analogues
- These are also **sometimes used post- operatively** to induce remission if surgery hasn't achieved this

- **Long-acting somatostatin analogues**
    - Octreotide and lanreotide
    - **Inhibit GH release.**
    - **Normalize IGF-1 in 75%**
    - Valuable role in reducing hypersecretion post-surgery.
    - Do not significantly reduce tumor size
    - These drugs are administered **subcutaneously**
    - **Side Effects:**
        - Gallstones from gallbladder stasis.
        - Steatorrhea
        - Abdominal Pain
        - Diabetes Mellitus
- **Dopamine agonists**
    - Cabergoline, bromocriptine
    - **Inhibit GH secretion**
    - Administered orally.
    - The size of the tumor is not reduced
    - **Useful for GH hypersecretion after surgery**
- **GH receptor antagonist**
    - Pegvisomant
    - For somatostatin analogue-resistant tumors
    - is a synthetic growth hormone receptor antagonist
    - **It lowers IGF-1 in >90% of patients**, which is accompanied by clinical benefits
    - Given S/C once weekly

- **Side Effects: Hepatitis**
- **Rapidly improves active symptoms.**
- Although **well tolerated**, it is **expensive** and has to be given subcutaneously.
- **It does not reduce tumor size.**

Remember:

- The **aim of treatment** should be **symptomatic control** and a **GH** concentration of **<5 mU/l.**

Criteria for cure of acromegaly:

1. **Normal IGF-1**
2. **+ Post-OGTT GH levels <1 µg/L**
3. **and/or Mean GH levels over 2 h <1 µg/L**

What are the indicators of disease activity?

- Symptoms such as headache and sweating
- HTN
- Skin tags
- Glycosuria
- Increased loss of visual fields.
- Peripheral edema

Mention some causes of macroglossia

1. Acromegaly
2. Amyloidosis
3. Hypothyroidism
4. Down syndrome.

What are the complications of acromegaly?

- Cardiomegaly and heart failure
- Hypertension
- Hypopituitarism
- Carpal tunnel syndrome
- Arthritis of the hip, knee and spine
- Spinal stenosis resulting in cord compression
- Visual field defects
- Increased risk of premalignant polyps and colon cancer: screening colonoscopy should be considered in all patients with growth hormone excess.
- **Hypercalciuria**
- **Hypertriglyceridemia**
- **Diabetes insipidus** (normally due to hypothalamic pressure effect; if there is impaired cortisol secretion symptoms may be masked
- Hyperthyroidism
- Impaired glucose tolerance (50%) and diabetes mellitus (10%)
- Cranial nerve palsies

- Tumors (uterine and colonic polyps are common; 10% develop malignant tumors)

Mention four common causes of death in such patients

This is proportional to the degree of GH excess.

- Cardiac failure and IHD
- Tumour expansion (mass effect and hemorrhages)
- Effects of hypertension
- Degenerative vascular disease
- Malignancy
- Apoplexy

What may be the significance of a raised calcium?

- **A raised calcium may indicate MEN 1**
    - Werner's syndrome
    - Inherited tumors: autosomal dominant, chromosome 11
    - 2 or more of pituitary tumor, islet cell tumor, parathyroid tumor, adrenal tumor
    - MEN2A medullary thyroid cancer (90%), pheochromocytomas (50%), parathyroid adenoma (20–30%)
    - MEN 2B medullary thyroid cancer (90%), pheochromocytoma, marfanoid habitus

What role is there for growth hormone in medical treatments?

- GH is used in childhood cases of short stature secondary to Turner's syndrome and GH deficiency but has no role in constitutional short stature.
- GH therapy in hypopituitarism improves
    1. well-being
    2. lipid profile
    3. bone mineral density
    4. possibly reducing cardiovascular mortality.

What are the complications of pituitary surgery?

- Diabetes insipidus (may be transient)
- SIADH (transient)
- Hypopituitarism
- CSF leak
- Intracranial bleeding – Stroke

What would you do if there was no mass seen in the pituitary fossa?

- Review the films with a neuro - radiologist, then arrange investigations to look for ectopic GH or GH-releasing hormone, e.g. pancreatic, adrenal, lung or ovarian neoplasia.

Figure 5.13 Prominent supra-orbital ridge. This patient has a clearly prominent supra-orbital ridge, as seen from the lateral view. This patient would be expected to be tall in stature and have 'coarse' facial features, with large hands. Further examination would include testing for a bitemporal hemianopia, cardiovascular examination and abdominal examination.

What is the pathophysiology of acromegaly?

- The most common cause is GH secreting **adenoma** of the anterior pituitary.
- At diagnosis, **75%** are **macroadenomas (>10 mm** diameter), and these account for one-third of all functional pituitary adenomas.
- Other **rare causes** include
    1. **Growth hormone-releasing hormone (GHRH) hypothalamic tumors**
    2. **Ectopic GH production** from carcinoid or small-cell tumors.

Endurance
20-08-2018

MRCP-PACES

Brief clinical consultation

ADDISON'S DISEASE

Scenario

- **Mr. Adam Hagger aged 46.**
- This gentleman has become **increasingly tired and fatigued of late**.

- Addison's disease (primary adrenal insufficiency) can either present with an **insidious and progressive course**, or with an acute **Addisonian crisis**.

Opening question:

- You got troubled with tiredness
- Could you tell me more about it?

Analysis of tiredness – fatigue?

ODPARA-OCD

- What do you mean by tiredness exactly?
- When did it start?
- Was it sudden or gradual
- Is it increasing, decreasing or same?
- **Any time during the day when tiredness is more?**

Differential diagnosis:

Addison's disease:

- Any dizziness when standing from sitting position
- Any tummy pains?
- Any skin pigmentation?
- Feeling sick or getting sick
- **Any cough? – TB**
- **Adrenalectomy**
- **Waterhouse–Friderichsen syndrome** (meningococcal sepsis and adrenal infarction)

OSA:

- Any snoring observed by others?
- Any daytime sleepiness?
- Any weight changes?

Anemia:

- Getting pallor than usual?
- Any blood loss?

PBC:

- Getting yellow discoloration of white f your eyes
- Any skin itchiness?

Chronic fatigue syndrome:

- Memory & concentration problems
- Headaches
- Tender lumps and pumps – LNs
- Sore throat
- Muscle aches - Myalgia
- Change in bowel habit - Irritable bowel

Metastasis:

- Pumps or lumps

Rule out Polyglandular syndromes:

- **Autoimmune primary adrenal failure** is **associated** with **several autoimmune conditions** and is part of **polyglandular autoimmune syndromes type I and II.**
- The **most frequent clinical sign** of associated autoimmune disease is **vitiligo**, which is found in **10-20%** of patients with **autoimmune adrenalitis**.

1. **Vitiligo**
2. **Type 1 diabetes**
3. **Pernicious anemia**: **pallor**, splenomegaly **– tummy pain,** polyneuropathy **- numbness**
4. **Hypoparathyroidism** – numbness in hands and feet or face
5. **Alopecia areata**: areas of **hair loss in scalp** with white, short, **tapering exclamation mark hairs**
6. **Rheumatoid arthritis**
7. **SLE**
8. **Sjogren's syndrome**: dry mouth and eyes

Drug History:

- Medication list
- Allergies

Family History:

- Significant illness

PMH:

- Any medical condition I should be aware of?
- Cranial radiotherapy

Surgical history:

- **Adrenalectomy -** Nelson's syndrome

Social History:

- What do you do for living?
- With whom you are living?
- **How much these symptoms affecting you at work and in daily living?**
- **Premature ovarian failure** is particularly associated with Addison's disease.
- Do you smoke?
- Do you drink alcohol?
- Any support needed at home
- Any financial support needed?
- **Travel abroad**

Can I examine you?

1. Medic alert bracelet

2. loss of hair:

- **Sparse body hair** (due to loss of androgens in complete adrenal failure).
- **In females**, **loss of axillary and pubic hair** (androgen-dependent hair).
- **In females the androgens are produced in the adrenal cortex**.
- This is **not affected in males**, as the **testes are the main source of androgens**

3. Hyperpigmentation of the skin

- **Present in 95%** of patients with **chronic primary hypoadrenalism**.
- **Normal skin does not exclude** the **diagnosis**.
- **Look for pigmentation in light-exposed areas** such as the **face and neck** and **pressure areas** such as the **elbows**, **knuckles**, and **shoulders** (**brassiere straps**), as well as **palmar creases**.
- **Hyper-pigmentation** also affects the **buccal mucosa**, **nipples axillae, perineum, and old surgical scars**.
- Remember, **pigmentation of the palmar creases** may be a **normal finding in dark-skinned** individual
- **Palmar creases** (normal in darkly pigmented people).
- **Lips and buccal membranes** – particularly bluish black discolorations.

- **Exposed and pressure areas** (feet, elbows, take off the patients watch and inspect around the belt and brasserie lines).
- If a patient has pigmented changes, secondary hypoadrenalism is unlikely.

4. Calcification of the auricular cartilage

- Occurs **exclusively in males** with **longstanding** primary or secondary **adrenal insufficiency**.
- It is **thought** to be a **consequence of longstanding glucocorticoid** deficiency and **does not resolve with steroid replacement**.

5. Bilateral adrenalectomy scars

- Examine for abdominal scars (especially of bilateral adrenalectomy; occasionally performed via an anterior (rooftop) approach).
- May **suggest previous surgical treatment for Cushing's disease**, and **consequent Nelson's syndrome**
- If bilateral adrenalectomy scars are present and the patient has diffuse tanning it is important to examine for visual field defect (looking for **bitemporal heminaopia**) – **Nelson's syndrome**

6. Visual fields: bitemporal hemianopia (pituitary adenoma)

- **Visual field defect** (classically bitemporal hemianopia) may be present if anterior pituitary function is compromised by an enlarged pituitary tumor such as a prolactinoma

7. Postural Hypotension:

- **Most patients** are **relatively hypotensive**, but **not all** demonstrate postural hypotension.
- Ask to **measure lying and standing BP**.

8. Auscultate chest

- The **second most common cause of primary adrenal failure** is tuberculosis.
- Tell the examiner you would like to **examine the lung fields** to look **for evidence of old tuberculosis (?apical lung signs).**

9. Be vigilant for **coexisting vitiligo**, as well as other autoimmune diseases e.g. thyroid.

What is your concern?

What is wrong with me?

- From what you told me and after I examined you, most likely you have inactive glands overlying our kidneys secreting important protein for body functions
- What we need to do is to arrange some blood tests and imaging to confirm diagnosis
- Will refer you to gland doctor and to social worker
- You will need long duration therapy called steroid; it is the substance that lacked due to loss of function of glands overlying your kidneys
- **We need to give you advices:**
    - Not to stand suddenly from sitting
    - You must wear medical alert bracelets to make others know that you have Addison's disease
    - You need to carry ampoule of cortisone with you to be given whenever your condition become unstable and whenever needed
    - You should be strictly adherent to your lifelong medications to avoid complications
    - When you get fever, loose motion, or become ill you need to duplicate your cortisone dose
    - You need to go to medical emergency immediately as your condition might be unstable and you may need urgent medical care
    - You need to do regular follow up to check your hormone level
    - By that you will live near normal life

Examiners' questions:

Present your findings please

- This male' patient has evidence of **widespread pigmentation**/ most marked in the **buccal mucosa**, **skin creases**, and **pressure areas**.
- There is also **calcification of the auricular cartilage**.

What is your diagnosis?

- The diagnosis is Addison's disease.

- There are **no adrenalectomy scars to suggest Nelson's syndrome**.
- I would like to examine for **postural hypotension** and look for **evidence of other autoimmune disease** and **previous tuberculosis infection**.

What is your differential diagnosis

Primary adrenal insufficiency

Addison's disease:

- **Pigmentation** due to a **lack of feedback inhibition by cortisol on** the **pituitary**, leading to **raised ACTH** and **melanocyte-stimulating hormone**
- In **80% of cases Addison's** disease is due to an **autoimmune** process.

Other causes include

1. adrenal metastases
2. adrenal tuberculosis
3. amyloidosis

Secondary adrenal insufficiency:

1. **Pituitary adenoma**
2. **Sudden discontinuation of steroid**

How you will investigate this case?

- **Short Synacthen**:
  - **Exclude** **Addison's disease** if cortisol rises to adequate levels
  - Test will **highlight failure of the adrenal glands** to produce enough cortisol.
  - **Blood cortisol** levels are sampled before, and at **30 and 60 minutes** after **250 µg of tetracosactide** (IM or IV).
  - A **normal response** is a **basal cortisol** in the reference range, a **cortisol rises of > 170nmol** above the basal result and/or a **peak cortisol > 530nmol/L**.
  - Note that a **random cortisol level,** although a useful indicator of adrenal function, **should not in itself** be relied upon as an accurate estimate of adrenal function.

- Severely **malnourished or septic patients** can have extremely low **plasma cortisol** levels as **cortisol is usually very highly protein bound**.

- **Long Synacthen® test**
  - **Diagnose Addison's disease** if cortisol does not rise to adequate levels
- **ACTH**:
  - Raised in primary hypoadrenalism.
- **Other blood tests:**
  - **Adrenal autoantibodies** (if autoimmune cause)
  - **Electrolytes**: hyponatraemia, hyperkalemia.
    - ↓ **Na+ (kidney loss)**
    - ↑ **K+**
    - ↑urea (dehydration)
  - **Blood glucose**:
    - ↓ **glucose**
  - **Eosinophilia**
  - **thyroid function tests** (hypothyroidism)
  - **CXR**: **Malignancy or TB**
- **8 am cortisol:**
  - No morning elevation suggests Addison's disease (**unreliable**)
- **Adrenal imaging (primary) and/or pituitary imaging (secondary) with MRI or CT**

How you will manage this case?

Acute (adrenal crisis)

- **0.9% saline IV rehydration** +++ and **glucose**
- **Glucorticoid replacement:**
  - **hydrocortisone** in divided doses classically **20mg in** the **morning**; **10mg at night** (see also Top Tips box)
  - Treatment may unmask diabetes insipidus (cortisol is required to excrete a water load)
  - **Titrate maintenance hydrocortisone** (and fludrocortisone) dose to levels/response
- **Mineralocorticoid replacement:**

- **fludrocortisone** for **postural hypotension**, may cause peripheral oedema.

- **Androgen replacement**:
  - may improve overall well-being and restore any decline in libido.

Anti-TB treatment increases the clearance of steroid, therefore higher doses required

Chronic

- **Education:**
  - **Compliance**
  - **Increase steroid dose if 'ill'**
  - **Steroid card**
  - **Medic alert bracelet**

What is the Prognosis of Addison's disease?

- Normal life expectancy

Anecdote

186.

- A candidate was asked to **look at a lady's hands.**
- He described Heberden's nodes, spindling of the fingers and proximal joint swelling, all of which the patient had.
- He suggested combined osteoarthrosis and rheumatoid arthritis.
- When the examiner asked about conditions associated with **rheumatoid arthritis**, the candidate looked beyond the hands and noticed the **generalized pigmentation** and then the **palmar crease pigmentation of Addison's disease**.
- The latter condition was the reason for the patient's inclusion in the examination – the joint changes had not been noted before!

Facial and buccal mucosa pigmentation

.

Palmar crease pigmentation.

Note pigmentation of the nipples and areolae.

Other questions commonly asked by examiners

What are the causes of primary adrenal failure?

1. **Autoimmune (70-90%)**
2. **Tuberculosis (10-20%)**
3. **Bilateral adrenalectomy**-usually for Cushing's syndrome or malignant disease
4. **Amyloidosis**
5. **Haemochromatosis**
6. **HIV**-due to associated CMV adrenalitis.
7. **Disseminated fungal infection**-e.g. histoplasmosis (common in the USA) and cryptococcus
8. **Hemorrhagic infarction**- associated with meningococcal septicemia (**Water mouse Friedrichsen syndrome**), other bacterial sepsis, anticoagulation, thromboembolic disease, and thrombophilia (anti-phospholipid syndrome)
9. **Adrenal metastases**- most commonly lung, breast, gastrointestinal, and melanoma
10. **Congenital-adrenal hyperplasia**

What other autoimmune endocrine disorders are associated with Addison's disease?

- **Half of patients with autoimmune adrenal failure** have an **associated autoimmune endocrine disorder**: By contrast, patients with type 1 diabetes mellitus, or Graves' disease, rarely develop adrenal disease.

Polyglandular autoimmune syndrome type 1

- This is a **rare autosomal recessive** disorder characterized by
    1. **Hypoparathyroidism**
    2. **Mucocutaneous candida** infection in **childhood**.
    - **Adrenal insufficiency** and **primary hypogonadism** develop during **adolescence**.

Polyglandular autoimmune syndrome type 2

- This **autoimmune condition** is **more prevalent than type 1** and is almost **universally associated with adrenal insufficiency**.
- **Half of the cases are familial**.
- **Autoimmune thyroid disease** and **type 1 diabetes mellitus** are also associated with -this condition.
- **Hypoparathyroidism** does **not occur** with this disorder.

What autoantibodies are present in primary autoimmune adrenal insufficiency?

- There are **3 antibodies** that have been described:
    1. Antibodies to **21-hydroxylase** (the **most common** and **specific**)
    2. Antibodies to **17-hydroxylase***
    3. Antibodies to **cytochrome P450** ((P-450 side chain-cleaving (P-**450scc) antibodies**)) *

    * These are **not as specific as antibodies to 21-hydroxylase** because they are **found in other tissues**.

What is the diagnostic test for adrenal insufficiency?

- **Single measurements of serum cortisol** may be **useful** in **excluding adrenal insufficiency** but are **not as sensitive as dynamic adrenal tests**.
- **A 9 am** measurement of **serum cortisol greater than 500 nmol/l** effectively **excludes adrenal insufficiency**.
- **Dynamic testing** is performed **if the 9am cortisol is equivocal**.

- This involves the administration of **250mcg of synthetic ACTH** (**synacthen**) and the **measurement of ACTH and cortisol before and at 30 and 60 minutes** after the **intravenous** administration of ACTH.
- If the test is performed at 9 am a **normal response at 30 minutes** is a **rise in cortisol over 550nmol/L**

Interpretation of an abnormal synacthen test:

- **Impaired cortisol response** and **ACTH >200ng/L-primary adrenal failure**
- **ACTH <10ng/L-secondary** (pituitary) **adrenal failure**

What is the treatment of adrenal insufficiency?

Adrenal crisis

- The management of acute hypoadrenalism involves **rapid steroid** and **fluid replacement**, and **reversal of electrolyte abnormalities**.
- If the **patient is not known to have adrenal insufficiency**, previously, **dexamethasone was considered the preferred steroid**, since it is **not measured in cortisol assays** and will therefore **not hinder subsequent diagnostic tests.**
- However, **hydrocortisone is the preferred** steroid since it has both **gluco - and mineralocorticoid actions**-subsequent **diagnostic tests are not affected if done more than 12 hours after the last dose of hydrocortisone**
- **Large volumes of 0.9% saline** are the preferred fluid, to correct hypovolaemia and hyponatraemia

Long-term management

- **Once the patient is stable**, the **diagnosis** of adrenal failure can be **confirmed with a synacthen test**, and the cause can be sought.
- The **long-term management** of primary adrenal insufficiency involves **glucorticoid replacement** with **hydrocortisone**, and **mineralocorticoid** replacement with **fludrocortisone**.
- Secondary adrenal failure does not require replacement with mineralocorticoid.
- The **patient must also be advised** of the serious nature of the condition, the need for **compliance with therapy** and the need to **increase dosing of hydrocortisone** (ant not fludrocortisone) **during illness and stress**.
- The patient should also be provided with a **'medic-alert' bracelet**.

Why does pigmentation occur in primary adrenal failure?

- ACTH is synthesized from a **precursor** called **proopiomelanocortin** (**POMC**).
- **POMC** undergoes **post-translational** processing to form either **ACTH, MSHs or lipotropins** (**LPHs**).
- Because of the **similarity in structure between ACTH and MSH**, abnormally **high concentrations of ACTH stimulate the melanocortin receptor**, causing **melanin deposition in skin** by melanocytes.

What is the differential diagnosis of skin pigmentation?

- **Addison's** disease
- **Nelson's** syndrome
- **Ectopic ACTH syndromes**
- **Haemachromatosis**
- **jaundice**
- **Uraemia**
- **Pregancy (melasma)**
- **Solar purpura**
- **Cafe au lait** spots
- **Venous eczema**
- **Porphyria cutanea tarda**
- **Fixed drug eruption**
    - **Tetracyclines**
    - **Barbiturates**
    - **Sulphonamides**
    - **NSAIDs**

What is the differential diagnosis of buccal pigmentation?

- **Addison's disease**
- **Melanoma**
- **Peutz-jehger's syndrome**
- **Leukoplakia**
- **Lichen planus**
- **Amalgam tattoo** (from adjacent amalgam dental fillings)

How common is adrenal insufficiency in HIV disease?

- **Adrenal insufficiency** is **common in HIV and AIDS**, affecting up to **15% of patients**.
    - This is **most often** due to **CMV-related necrotizing adrenalitis**
    - May also be caused by **infection** with:
        - **Mycobacterium avium complex**
        - **Cryptococcus neoformans**

- **infiltration by Kaposi's sarcoma**.
- **Drugs used to treat opportunistic infection in HIV** disease may also cause adrenal insufficiency.
    - **Ketoconazole inhibits cortisol synthesis**
    - **rifampicin increases cortisol metabolism** through enzyme **induction**.

How common is adrenal insufficiency in septic shock?

- Almost **half of patients with septic shock** have an **abnormal response to synacthen**, and these patients seem to have a **worse outcome** than those with preserved adrenal function.
- However, there is **conflicting evidence** regarding the **benefit of** treating these patients with **low dose hydrocortisone**.

What are the causes of hypoadrenalism?

Primary:

- **Autoimmune adrenalitis**
- **Granulomatous**: TB, histoplasmosis, sarcoidosis
- **Amyloidosis**
- **Haemochromatosis**
- **Metastatic** infiltration
- **Thrombotic** disease
- Congenital adrenal hyperplasia
- **Adrenoleukodystrophy** (**rare, X-linked** inherited disorder therefore, **more common, and severe in males**, resulting in **progressive brain damage**, **failure of the adrenal glands** and eventually **death**)
- **Iatrogenic**: following **bilateral adrenalectomy**

Secondary:

- **Anterior pituitary failure**.

How may a patient with an acute Addisonian crisis present?

- Addisonian crisis is often characterized by **nausea and vomiting** with accompanying **hypotension**.
- **Hypoglycemia** and **confusion** may or **may not be present**.
- If **cardiovascular compromise** is significant, the patient **may present** in **shock** and may be **centrally cyanosed**.

What diseases are associated with Addison's disease? (listed in order of frequency)

1. Vitiligo
2. Autoimmune thyroid disease (Hashimoto's and Graves')
3. Diabetes mellitus
4. Pernicious anemia
5. **Coeliac disease**
6. **Premature ovarian failure**
7. **Hypoparathyroidism**.

What are the polyglandular autoimmune syndromes?

Type I:

- **Mild immune deficiency** (causing **chronic mucocutaneous candidiasis**), **hypoparathyroidism** and **Addison's disease**.
- Patients may also have **other organ-specific autoimmune diseases.**
- Due to **mutations in the autoimmune regulator** (AIRE**) gene.**

Type II (Schmidt's syndrome):

- **Addison's disease, type 1 diabetes mellitus** and **thyroid disease** (**hypo or hyperthyroidism**).
- NB Do not confuse the autoimmune polyglandular syndromes with the multiple endocrine neoplasia syndromes

What is the mechanism of hyperpigmentation in adrenal failure and can you name some other causes of hyperpigmentation?

- The pituitary gland produces a pre-hormone called **proopiomelanocortin** which is **cleaved to ACTH and MHS** (**melanocyte stimulating hormone**).
- In adrenal failure, the negative feedback loop of adrenal hormones (especially cortisol) on the pituitary is lost, therefore the ACTH precursor is produced in excess, leading to higher than normal levels of MSH.
- MSH stimulates melanocytes resulting in pigmentation.

Other causes of hyperpigmentation include:

- **Racial**
- **Sun exposure**
- **Uraemia**
- **Haemochromatosis**
- **Primary biliary cirrhosis**
- **Porphyria cutanea tarda**.

What is Nelson's syndrome?

- Nelson's syndrome is the rapid enlargement of a pituitary adenoma accompanied by remarkably high ACTH levels and hyperpigmentation (due to excess pro-opiomelanocortin production).
- The tumor may compress the optic chiasm causing visual field defects.
- It can occur after bilateral adrenalectomy for Cushing's disease, with loss of the negative feedback loop.

Who was Thomas Addison and why is he so famous?

- Thomas Addison was a physician of great renown in the 19th century, who described the following conditions, either alone or in collaboration with others:
    - Addison disease * and Addisonian crisis
    - Pernicious anemia (eponymously known as Addisonian anemia)
    - Adrenoleukodystrophy (known as Addison–Schilder syndrome)
    - Primary biliary cirrhosis (known as Addison–Gull syndrome)
    - Allgrove syndrome (isolated glucorticoid adrenal failure, achalasia and alacrima – described by Allgrove and colleagues 1 more than a century after Addison)
    - Addison's keloid syndrome (now known as morphea)
    - Appendicitis.
    - (* NB Addison's first description of adrenal failure was in the context of TB of the adrenal glands. 2)
    - He suffered from tremendous bouts of depression and committed suicide in 1860, shortly after his retirement.

What are the causes of primary hypoadrenalism?

- **Autoimmune adrenalitis**
- **Tuberculosis** (in endemic areas –? lung signs)
- **Bilateral adrenalectomy** (malignant disease, e.g. breast cancer, Cushing's syndrome)
- **Secondary deposits**
- **Amyloidosis** (hypoadrenalism preceded by **nephrotic syndrome**)
- **Haemochromatosis**
- **Granulomatous** disease (rarely **sarcoidosis**)

- **Fungal diseases** (e.g. histoplasmosis)
- **Congenital adrenal hyperplasia***
    - *Series of inherited **defects in adrenocortical steroidogenesis** (e.g. 21-hydroxylase deficiency).
    - **Homozygotes present neonatally with salt wasting**, **hypotension,** and **ambiguous genitalia** in **females**.
- **Meningococcal and pseudomonal septicemia**
- **AIDS**
- **Adrenal hemorrhage** (newborn, especially breech delivery; patients on anticoagulants)
- **Adrenal vein thrombosis** after trauma or adrenal venography

What are the causes of skin pigmentation?

- Is **usually racial** (including buccal pigmentation) or due to **sun-tanning**.
- **Other causes** of abnormal generalized pigmentation include the following:

- **Endocrine**
    - **ACTH therapy** (e.g. **asthma**)
    - **Cushing's disease** (? facies, truncal obesity, striae, etc.;)
    - **Thyrotoxicosis** (? exophthalmos, goitre, etc.)
    - **Ectopic ACTH** (especially **oat cell carcinoma**)
    - **Uncontrolled congenital adrenal hyperplasia**.
    - **Chronic debilitating disorders** (also, like Addison's, associated with lassitude and weight loss)
    - **Malignancy** (including reticuloses and leukemias)
    - **Malabsorption syndromes**
    - **Chronic infections (especially TB)**
    - **Cirrhosis** (? icterus, spider naevi, etc.)
    - **Uremia** (pale, brownish-yellow tinge to skin)

Pigments other than melanin such as:

- **Haemochromatosis** (slate-grey pigmentation, hepatosplenomegaly, etc.)
- **Argyria**
- **Chronic arsenic poisoning**.
- **Drugs**

- **Phenothiazines** (blue-grey pigmentation)
- **Antimalarials** (blue-grey pigmentation)
- **Amiodarone** (grey pigmentation)
- **Cytotoxics**
- **Minocycline** (purple-blue pigmentation; may get **blue oral discoloration due to blue-black discoloration** of **alveolar bone and hard palate** – '**black-bone disease'**)

Endurance

30-10-2018

MRCP-PACES

Brief clinical consultation

Adrenal incidentaloma

You are SHO in endocrinology clinic
Mary is a 40 years old female
Underwent routine insurance medical checkup and found to have (3x4 cm) mass in right suprarenal gland
She is asymptomatic

Background and opening question

- We are here today to discuss some issues related to what was found in imaging done for you
- A mass of 3x4 was found in the gland overlying your right kidney
  Could you tell more regarding that?
- May I ask you some questions that might clarify things more and help us in our discussion today

Screen for differential diagnosis:

- **Metastasis:**
  - Weight loss
  - High body temperature
  - Bumps and lumps
- **TB:**
  - Cough
  - Contact with sick patient
- **Adrenal cancer:**
  - Excessive body hair
- **Pheochromocytoma:**
  - Handshake
  - Hand sweating
  - Feeling anxious
  - Heart racing
- **Adenoma:**
  - **Cushing's**
    - Weight change
    - Skin change

        - Mood change
    - **Conn's**
        - Muscle weakness

DH:

- Medication list
- Allergies

PMH:

- History of cancer
- Any medical condition I should be aware of?

Social:

- What you do for living?
- Smoking
- Alcohol

Can I examine you?

- Observations chart:
    - BP, PR
- General appearance
- Facial appearance
- Skin - hair, skin changes
- Hand sweating
- Test for proximal myopathy

Concern:

What's wrong with me?

- From what you told me and after I examined you, most likely you have a condition called **adrenal incidentaloma**
- This is a medical term in which a lesion is discovered by chance only in gland overlying your kidney where imaging is done for other reason
- Mostly it gives no symptoms
- What we need to do is to arrange further imaging and tests to confirm our diagnosis and to rule out others
- No need for admission
- Will arrange appointment after requested tests result to discuss you the plan of management which may include referral to gland doctor dependent on results
  Is that okay with you
- Do you have any other concern?

I am very worried, is it cancer?

- I sorry for what you feel now
- Cancer possibility is very minimal but it's still possibility and needs to be ruled out

Examiners' questions:

What is your findings?

- Honestly, I picked no abnormality in clinical examination
- Nor in observation chart neither in systemic examination

What is your diagnosis?

- Most likely adrenal incidentaloma

What are your differential diagnoses?

1. Adrenal cyst
2. Adrenal adenoma
3. Adrenal lipoma
4. Adrenal carcinoma
5. Metastatic deposit
6. TB
7. CAH - But mostly bilateral

How you will investigate this patient?

- **Basic investigations**
- **Investigations looking if this suprarenal mass is functioning or not**
- This included:
    - **Cortisol secreting adenoma - Cushing's:**
        - 1mg overnight dexamethasone suppression test
    - **Aldosterone secreting adenoma - Conn's:**
        - Aldosterone/renin ratio (ARR)
    - **Carcinoma**
        - **Measure sex hormones and steroid precursors:**
        - DHEAS
        - Androstenedione
        - 17-OHP and testosterone in women
        - estradiol in men and postmenopausal women
    - **Pheochromocytoma**
        - Urinary metanephrines
        - Plasma free metanephrines
    - **CAH:**
        - Mostly bilateral
        - 17- OHP
- **Radiology:**
    - **A- Non contrast CT - adrenal protocol:**
        - Measures density in **Hounsfield units**
            - If >10 HU – these therefore overlap in density with malignant lesions and Pheochromocytoma
    - **B- +/- MRI adrenal**

- **Adrenal biopsies:**
  - Rarely done for patient with history of extra-adrenal malignancy and Indeterminate radiology result

How you will manage this patient?

- **Surveillance** follow up
- **Surgery** to be considered in the following:
  1. **Masses ≥4.0 cm**
  2. Regardless of size, any incidentaloma with clinical, radiologic, or hormonal abnormalities **indicative of adrenal malignancy or hyperfunction** should be considered for surgical removal
  3. Adrenal incidentaloma that **increases in size** may be considered for surgery.
  - If surgeon skill and lesion characteristics allow, **laparoscopic adrenalectomy** should be the surgical technique of choice (Level 3 Evidence, Grade C Recommendation).
- **Recommended follow-up:**
  - **Small masses**
    - Consider no follow up
    - Enrollment in a clinical trial
  - **Clinical and hormonal follow-up** using screening tests employed at initial evaluation **annually for 4 years**
  - **A single follow up imaging investigation at 3–6 months** for suspicious masses **or at 12 months** for apparently benign lesions.
  - Patients with tumors that remain stable on imaging and annual hormonal evaluation may be considered for discharge from follow-up after 4 years

MRCP-PACES

Brief Clinical Consultation

Anderson Fabry's disease

Angiokeratoma corporis diffusum

You are SHO in the clinic today
Mr. Edwardo is 34 years old
Complaining of skin rash

Confirmations:

- **Self**
- **Patients**
- **Agenda**

Opening question:

Empathy and sympathy:

Brief analysis of skin rash:

- **Where is the rash exactly?**
- **ODPARA**
  - Onset
  - Duration
  - Progression
  - Association
    - Attacks of excruciating unexplained pain hands and body
  - Relieving factors
  - Aggravating factors
  - Any itchiness?
  - Any ooze?
  - Is it painful?
- **Can I see it?**
  - **Any joint pain**
  - **Heart:**
    - Any chest pains
    - Any heart racing
  - **CNS:**
    - Any weakness
    - Any sensory impairment

- **Kidney:**
  - Any frothy urine?
  - Any blood in urine?

Drug history

- Any medications
- Any allergies

Family history:

- Similar condition

Past medical history:

- Any illness I should be aware of

Social history:

- What do you do for living?
- QOL - causing stress or stigma
- Smoking
- Alcohol

Can I examine you?

- **The skin**
  - **Macules and papules** with fine, keratotic crusts = Groups of **darkish-red** and **black** telangiectatic macules and papules - **angiokeratomata**, about **2–4mm** in diameter, **over the thigh and around the limbs**, **buttocks**, around the umbilicus (**periumbilical rosette**), lower **trunk** and on the **shaft of the penis**
  - The papules do **not fade on pressure**
- **Eye:**
  - **Conjunctival injection**
  - **Dilated and tortuous vessels**
  - Superficial **corneal dystrophy**: - **Cornea verticillata**- which is almost **specific** to this condition
- **CVS - Murmur**
- **CNS - TIA:**
  - Weakness
  - Sensory impairment
- **Joints:**
  - Arthropathy of the terminal interphalangeal joints.
- **BP: Mild hypertensive**
- **Lower limbs:**
  - Varicose veins
  - Stasis edema

What is your concern?

- From what you told me and after examining you, most likely you have a medical condition called Fabry's disease

- It's a **disease run in family**, causing **accumulation of substance in your skin and internal organs** leading to symptoms you have
- We need to do some tests, heart tracing and imaging to confirm it
- It's controllable and not curable
- **Will refer you to geneticist** and will offer **genetic counseling** to family members if agreeing
- Will refer you to group of specialists to deal with your problem if you got any internal organ affection
- **Is that okay with you?**

Examiners' questions:

What is your diagnosis?

- Anderson Fabry's disease

How to investigate this case?

- **Basic investigations:**
  - RFT, electrolytes
- **Complications:**
  - ECG
  - Echocardiogram
  - Cardiac MRI
  - Urinalysis
  - Urine proteins
  - **Formal ophthalmological assessment**

Confirm diagnosis:

- Blood test that measures the activity of **alpha galactosidase**
- Enzyme assay - usually done on leukocytes
- **Genetic testing** - particularly in females

How are you going to manage this case?

- **Enzyme replacement therapy**
- **Not a cure**
- Can partially prevent disease progression, as well as potentially reverse some symptoms
- **Gene therapy treatment**
- **Organ-specific treatment**
  - **Analgesics**
  - **Anticonvulsants**
  - NSAIDs - avoid in CKD
  - ICD
- **Clinical trials**

Clinical Notes

- **Lysosomal storage disease**
- **X- linked recessive**
- Causes a **glycolipid** known as **globotriaosylceramide** (abbreviated as **Gb3**, **GL-3**, or ceramide trihexoside) to **accumulate within the blood vessels**, other **tissues, and organs.**
- This accumulation leads to an **impairment of their proper functions**.
- Most cases of Fabry's disease occur in males and **the female carriers are mostly symptomless.**
  incomplete penetrance in heterozygous females.
- **The condition affects hemizygous males** (i.e. all males), as well as homozygous, and in many cases heterozygous females.
- **While males typically experience severe symptoms**, women can range from being asymptomatic to having severe symptoms.
- **Symptoms:**
  - **Full body or localized pain** to the extremities known as **acroparesthesia or (GI) tract** is common.
  - This acroparesthesia is believed to be related to the damage of peripheral nerve fibers that transmit pain.
  - GI tract pain is likely caused by accumulation of lipids in the small vasculature of the GI tract which obstructs blood flow and causes pain
  - **CVS:**
    - The accumulation of sphingolipids within heart muscle cells causes **abnormal thickening of the heart muscle** or **hypertrophy**.
  - This hypertrophy can cause the heart muscle to become abnormally **stiff** and unable to relax, leading to a **restrictive cardiomyopathy**
  - **Conductive defect:**
    - **Complete heart block**
    - Ventricular **tachycardia**.
    - These can cause sudden **cardiac death.**
  - Sphingolipids can also build up within the **heart valves, thickening** the valves.
  - If severe, this can cause **valvular regurgitation or stenosis**
  - The **aortic and mitral valves** are more commonly affected than the valves on the right side of the heart
  - **Skin:**
    - The cutaneous eruption first appears at, or soon after, puberty.

- **Angiokeratomas** - tiny, **painless papules** that can appear on any region of the body, but are predominant on the thighs, around the umbilicus, buttocks, lower abdomen, and groin
- **Anhidrosis**
- **Hyperhidrosis**

- **Raynaud's disease**-like symptoms with neuropathy
- **Ocular involvement**:
  - **Cornea verticillata** - vortex keratopathy i.e. clouding of the corneas.
  - **Keratopathy**
  - This clouding **does not affect vision.**
  - Conjunctival and retinal vascular abnormalities
  - Anterior/posterior spoke-like cataract
  - Visual reduction
- **CNS:**
  - Fatigue
  - Neuropathy, **burning extremity pain**, red hands and feet
  - Increased risk of stroke - **early strokes**, mostly vertebro-basilar system
- **Kidneys:**
  - **Albuminuria**
  - **Hematuria**
  - Specific lipophages may be seen in the urine resulting from lipid infiltration of the glomerular vessels
- **Others:**
  - Tinnitus, vertigo
  - Nausea, inability to gain weight, diarrhea
  - New research suggests many women suffer from severe symptoms ranging from **early cataracts** or strokes to hypertrophic left ventricular heart problems and **kidney failure**.
  - This variability is thought to be due to X-inactivation patterns during embryonic development of the female.

- **Diagnosis:**
  - **Clinical presentation**
  - **Enzyme assay** - usually done on leukocytes to measure the level of alpha-galactosidase activity.
  - **Molecular genetic analysis** of the **GLA gene** is the most accurate method of diagnosis in females, particularly if the mutations have already been identified in male family members
  - **Cardiac MRI:**

    - Accurate in accessing left ventricular mass and thickness and hypertrophy
- **The prognosis:**
    - Usually grave
    - **Death** occurring in the **third or fourth decade** from a **vascular accident or uremia**

MRCP-PACES

Brief Clinical Consultation

Ankylosing spondylitis - Back pain

Role: Medical registrar in outpatient clinic
Mr. Edwardo is 36 years old gentleman, has been complaining of **severe back pain** over the last 3 years following a **road traffic accident**
This has progressively got worse, now requiring higher doses of simple analgesics.
His **back pain is worse in the mornings** and improves with analgesics by the afternoon.
He uses paracetamol and ibuprofen regularly. Over the last 3 months he has noticed **increasing breathlessness on exertion**, with a noticeable reduction in exercise tolerance. He has no other significant medical history.
Thank you for your assessment
Task: Assess the patient and determine the causes for symptoms.
Advise on further investigation and treatment

Confirmation:

- Self
- Patient
- Agenda

Background:

- You got troubled with back pain
  Could you tell me more about it?
  - yes doctor, I have this low back pain for 3 years, it's really awful

Empathy and sympathy:

Analysis of back pain:

ODPARA

- When did it start?
- Sudden or gradual
- Is it same, improving or worsening?
- Anything relieving it?
- Anything worsening it?
- Constant or intermittent?
- **Any radiation?**
- **Is it related to exertion?**
- **Is it present at rest?**
- **Any trauma?**

        - RTA
        - No fracture
        - X ray normal
- Water work control
- Back passages control
- Weakness
- Loss of sensation in legs
- **Any time during the day pain is at the worst?**
        - Worse in the morning
        - Difficult getting out of bed
        - Improves as day goes on
- In scale of zero to ten how much you score your pain
- **Any joint pain**
- Any other joints affected?
- **Any stiffness**
- **Skin rash**
- **Associated symptoms**

        - Over the last 3 months you have also noticed increasing **breathlessness on exertion**
        - **How many flights of stairs you can go before getting SOB?**
        - Any chest pains
        - Any dizziness
        - Ankle swelling?
        - Orthopnea?
        - Paroxysmal nocturnal dyspnea?
        - **Exercise tolerance**

Differential diagnosis:

- **Discitis**
        - High body temperature
        - Unpasteurized milk
        - Contact with animals
- **TB**
        - History of travel
        - Contact with sick patient
- **Malignancy**
        - Weigh loss
        - Pumps and lumps
- **Rheumatological**
        - **Rheumatoid arthritis**
        - **Seronegative arthritis:**
            1. Psoriatic arthritis
            2. Enteropathic arthritis

3. Ankylosing spondylitis
4. Reactive arthritis

Drug history:

- Any allergies
- Medication list
- Paracetamol and ibuprofen

Past Medical History:

- **Are you suffering from any medical condition?**

Social history:

- Job
- QOL
- Smoking
- Alcohol

Family history

- My mother suffers with severe **rheumatoid arthritis**

Can I examine you?

- **Ask patient to stand:**
    - **Kyphosis** - **question-mark posture**
    - **Decreased spinal movements**
    - **Tenderness over sacroiliac joints** - checked with patient and examiner
    - **Flesche's test** - increased occiput-wall distance
    - **Modified Schober's test** - do not need to perform in examination
    - **Arthritis of other joints**
        knees
        Hips
- **Examine pulse:**
    - **Bradycardia** - **heart block**
- Check blood pressure
- **Wide pulse pressure AR**
- Examine chest:
    - **Reduced chest expansion**
    - **Apical lung fibrosis**
- Examine the heart:
    - **AR**
    - **? MR**
- Assess JVP
- Elevated in HF:
- **Cardiac failure** could be due to
    - **severe aortic regurgitation**
    - restrictive cardiomyopathy (secondary to amyloidosis)

- **Ankle edema:**
- Could be caused by
    - congestive cardiac failure
    - amyloidosis (nephrotic syndrome)

What are your concerns?

What's wrong with me?

- From what you told me and after examining you, most likely you have a condition called **Ankylosing spondylitis** in which there is defect in own body defense system attacking joints and lung and various organs in your body causing the symptoms you have
- What we need to do is **up-titrating analgesic medications**, to arrange some blood tests and imaging, refer you to group of specialists including physiotherapist, and exercise trainer and will refer you to joint doctor, lung and heart doctors
- Will arrange clinic follow up to relay the above results and to monitor you
- Is that okay with you?

Do I have rheumatoid arthritis?

- The **symptoms do not suggest rheumatoid arthritis**, as other features of rheumatoid arthritis are not present on examination.

What is the cause of breathlessness?

- The **deformity of the chest wall** can cause breathlessness.
- However; ankylosing spondylitis **can affect other organs** such as the **heart** and **lung**, and this-may cause breathlessness.
- Although the exact cause of breathlessness is not clear, this warrants further investigation

Examiners' questions:

What is your diagnosis?

- Ankylosing spondylitis

What are your differential diagnoses?

- The differential diagnosis of **morning back pain:**
    1. **RA**
    2. **Ankylosing spondylitis**
- The differential diagnosis for **exertional breathlessness** in a patient with **ankylosing spondylitis** is:
    1. **Chest wall deformity** and reduced chest expansion
    2. **Aortic regurgitation**
    3. **Heart block**
    4. **Apical pulmonary fibrosis**
    5. **Amyloidosis** with **nephrotic syndrome** (**pleural effusions**)
    6. **Amyloidosis** with **restrictive cardiomyopathy**

How you will investigate this case?

- **Basic investigations:**
  - CBC
  - Electrolytes
  - Inflammatory markers
  - RF
  - **Atrial NP:**
    - ✓ Normal levels are less than 100 pg/ml.
    - ✓ It has a negative predictive value of at least 96%, so cardiac failure (due to systolic or diastolic dysfunction) can be confidently ruled out for patients in the normal range.
  - ECG
  - Echocardiogram
  - 24hr halter monitor
- **Imaging:**
  - CXR
  - X-ray of pelvis and spine
  - **XR sacroiliac joint:**
    - A plain X-ray is usually sensitive enough to demonstrate sacroiliitis, and **severity is graded from 0 (normal) to IV** (fused).
    - If this is normal, but suspicion remains high, **MRI** is warranted, since it is the **most sensitive and specific** investigation **for sacroiliitis.**
  - **Lung function tests - restrictive defect**
  - **HRCT chest - lung fibrosis**
  - **Urinalysis:**
    - Proteinuria may indicate **amyloidosis** (nephrotic syndrome).
    - If proteinuria is present, this can formally be quantified with a 24-hour urine collection.

Further management

- **Patient education**
- **Exercise** and **physiotherapy**
- Up titrate **analgesia**
- Disease modifying anti-rheumatic drugs (**DMARDS**) (methotrexate and sulphasalazine) have no role in **spinal disease** but can be used for peripheral disease
- Biological therapy **anti-TNFa therapy** (**adalimumab and etanercept**) can be used for **active spinal disease** not responding to ~2 NSAIDs (NICE guidelines)

MRCP-PACES
STATION 5
ANKYLOSING SPONDYLITIS

Scenarios

- SOB
- Back pain
- Eye redness or pain
- Palpitation
- Low back pain and stiffness
- Exertional dyspnea (pulmonary fibrosis)

Hello
I am doctor…
One of the doctors in the clinic today
Are you Mr.……

Opening question

I understand that you have been troubled with back pain, could you tell me more about that?

Brief analysis of complain

SOB

- When did it started exactly?
- How many steps you can manage before getting SOB?

Redness in eyes

- Is it in one or both eyes?
- Any diminution of sight?
- Eye discharge

Back-pain

- Onset, duration, severity, variation, exacerbating and relieving factors, radiation, morning stiffness, effect on life? (pain is worse at night and morning with stiffness, exercise helps it)

Frame of ankylosing spondylitis:

Can I ask you some questions?

- Any joint pain
- Red painful eye denoting anterior uveitis
- Any neck pain denoting kyphoscoliosis
- Any heart racing denoting aortic regurgitation or chest pain
- Any SOB denoting apical fibrosis, restrictive lung disease or aortitis
- Any frothy water work denoting amyloidosis
- Any back- pain?
- Any ankle pain denoting Achilles tendinitis

Focused history of presenting illness:

- Any other joints involved?
- Heel pain?
- Red eyes
- Sob (pulmonary fibrosis)
- AR (palpitations, SOB, leg swelling)
- IBD-Bowel habits, mouth ulcers?
- Skin rash (psoriasis)
- Any trauma? Fever?
- Alarm symptoms- spinal cord compression?

Medication history:

- NSAIDs? Any side effects?

Any medical condition I should be aware of?

JSD:

- How these symptoms affecting you in daily activity and in job?
- With whom you are living?
- Sick leave
- Stop smoking
- Stop driving due to affection of your neck

Examination:

Inspect:

- Pulse – collapsing, ask for pain in shoulder
- Can you stand up please?
- Remove shirt to examine the back
- Come from side of patient and inspect from above down
    - Hyper extended neck
    - Kyphoscoliosis
    - Loss of lumbar lordosis
- Ask to walk – other patient you ask to walk are short and long stature patient
- Ask to walk- question mark, Stooped posture? Loss of lumber lordosis and exaggerated thoracic kyphosis and neck hyperextension, protuberant abdomen
- **Check cervical movements**
- Check low back movements (fix the patients pelvis before the movements)
- auscultate lung apex for pulmonary fibrosis
- Basal crackles
- heart for AR, pacemakers (conduction blocks)?
- Eyes for anterior uveitis
- Ask to perform **modified Schober's test**
- occiput wall distance test
- ask to check chest expansibility
- Urine dip for proteinuria (amyloidosis, NSAID induced
- nephropathy)

Lower limb edema:
Two-minute warning

Any concern?

What is wrong with me doctor?

- From what you told me and after examining you
- You have a condition called ankylosing spondylitis
- I t is a medical term for a medical condition in which there is multisystem involvement with scaring in lung causing your SOB
- What we need to do now is to do some blood tests and imaging to confirm the diagnosis and to rule out others

- You might have a condition called ankylosing spondylitis where your own immune system is mistakenly attacking the spine and other joints leading to pain and stiffness
- For your pain, we will start with pain killers/anti-inflammatory agents and will ask physiotherapists to see you
- We will do some blood tests (inflammatory markers) and obtain an X ray of your back and also MRI scan of your back
- I will refer to joint doctor who can start you with medication to dampen down the immune system, also will get help of occupational therapists
- Inform the employer about diagnosis for work adjustments
- 15-20% chance to get it if 1st degree relative has it, 2% chance if HLA B27 positive
- Info about support groups

Present your findings

- This gentleman is having features suggestive of ankylosing spondylitis
- There is reduced movement of neck and trunk
- I could not appreciate eye redness
- There is loud P2

What are the differential diagnoses?

Inflammatory back pain

DD of low back pain and stiffness:

1. Ankylosing spondylitis
2. Other seronegative arthritis (psoriatic, enteropathic, reactive)
3. Rheumatoid arthritis
4. Osteoarthritis

What are differential diagnoses of eye redness?

1. Anterior uveitis
2. Conjunctivitis

Extra-articular features:

- Anterior uveitis
- Apical pulmonary fibrosis
- AR, Aortic conduction blocks

 Atlanto-axial subluxation
 Achilles tendinitis
 Amyloidosis, IgA nephropathy

Investigations:

 Inflammatory markers-ESR, CRP, CBC (anaemia)
 HLA B27
 RFT (for Amyloidosis)
 X ray of LS spine and sacroiliac joint
 MRI of LS spine and sacroiliac joint
 CXR, Pulmonary function tests, HRCT for Pulmonary fibrosis
 ECHO for AR

Treatment:

- MDT approach
- Exercise, physiotherapy, occupational therapy
- NSAIDs (1st line), intraarticular steroids
- **DMARDs** (sulphasalazine) may be effective in peripheral arthritis
- **Biological agents** -Anti-TNF alpha therapy (etanercept, adalimumab)
- Surgical-hip replacement

MRCP-PACES

Brief Clinical Consultation

Cataract

You are a doctor in the clinic today
Mr. Arthur, 70 years old complaining of diminution of vision
Please advice
Yours, GP

Confirmations:

- Self
- Patient
- Agenda

Checks:

- Understanding
- Expectations
- How he feels

Opening question:

- I got a letter from your GP mentioning you have problem eye sight
- Can I get from you more information about that, please?
- Yes doctor, since last 8 weeks I started to have difficulty in reading and watching the TV , it is getting worse since then

Empathy and sympathy:

Brief analysis of the diminution of vision:

What do you mean exactly?

- I can't see clearly

ODPARA:

- Is it sudden or gradual?
- Anything increasing it?
- Anything improving it?
- Any problem with night vision
- Do you use glasses?
- When you did last time checked your sight?
- Any jaw pain?
- Any pain in temples
- Any headache?
- Any skin rash
- Any joint pain?

Differential diagnosis:

- Any trauma to eyes?

- Any high blood sugar?
- **Cushing's syndrome:**
    - Any weight change
    - Any high blood pressure
    - Any skin thinning or bruising?
- **Hypoparathyroidism:**
    - Any weakness?
    - Any heart racing?
- **Malignancy** – treatment:
    - Any high temperature
    - Any weight loss
    - Did you receive any radiotherapy?

PMH:

- Any medical condition I should be aware of
- Any high blood sugar?

FH:

- Similar conditions

Drug history:

- Show me your medications list
- Any drug allergies?

Social history:

- What do you do for living?
- How much these symptoms affecting you at work and on daily life activity
- Smoking
- Alcohol
- **Driving** – you don't need to stop driving or inform DVLA if you have minimal requirement for driving which are no alteration in visual field , acuity 6/12 for small cars and at least 6/60 for buses and lorries and you can read car plates from 20 meters

Can I examine you?

- Visual acuity
    - The **visual acuity is reduced** in both eyes
- Fundoscopy
- There is **lens opacity** visible in the right eye
- **Red reflex**
    - Diminution of the red reflex.
    - A black opacity is seen in the lens against o reddish hue of the reflex.
    - This moves upwards on upward gaze
- Check finger pulps for blood sugar checking

What is your concern?

- **What is wrong with me?**
- From what you told me and after examining you, most likely you have a condition called senile cataract

- Cataracts are when the lens, a small transparent disc inside your eye, develops cloudy patches.
- Over time these patches usually become bigger causing blurry, misty vision and eventually blindness.
- When we're young, our lenses are usually like clear glass, allowing us to see through them.
- As we get older, they start to become frosted, like bathroom glass, and begin to limit our vision.
- What we need to do now is to refer you to eye doctor for best plan of care and to social worker and occupational therapist for advices
- We will arrange some blood tests and will need to do formal optician assessment
- Is that okay with you?

What are your findings?

- Bilateral lenses opacity
- Reduced visual acuity bilaterally
- With diminished red reflexes

What is your diagnosis?

- **Bilateral senile cataract** - located in the anterior half of the lens

What are your differential diagnoses?

1. **Senile cataracts**
2. **Medications induced**
3. **Trauma-** less likely since it is bilateral and no history of trauma
4. **Infections –** Cysticercosis, Onchocerciasis and Toxoplasmosis

Questions commonly asked by examiners

What are the causes of cataracts?

Congenital

- Toxoplasmosis
- Rubella
- CMV
- HSV
- Syphilis
- Myotonic dystrophy
- Homocystinuria
- Down's syndrome
- Patau's syndrome
- Edward's syndrome
- Turner's syndrome
- Alpert's syndrome
- Fabry's disease
- Wilson's disease
- Refsum's disease

- Bardet-Biedl syndrome
- **Autosomal dominant** trait

Acquired

- **Age**
- **Trauma**
- **Uveitis**
- **Diabetes**
- **Cushing's** syndrome
- **Hypoparathyroidism**
- **Radiation**
- Cysticercosis
- Onchocerciasis
- Toxoplasmosis
- Leprosy
- Atopic dermatitis
- **Drugs**

What drugs can cause cataracts?

Drugs most commonly implicated:

- **Corticosteroids** (oral, intravenous, topical and inhaled)
- Chlorpromazine
- **Chloroquine**
- Busulphan
- Chlorambucil
- **Others drugs (weak association):**
    - **Tamoxifen**
    - Tricyclic antidepressants
    - Potassium-sparing diuretics
    - **Amiodarone**
    - Tetracyclines
    - Allopurinol
    - Psoralens

What is the treatment for cataracts?

Intra-capsular cataract extraction (ICCE)

- This involves **extraction of t he whole lens** including the posterior capsule, and **placing the artificial lens** in the anterior chamber or suturing it to the posterior chamber.
- **Advantages:** abolishes the risk of subsequent capsular opacity and less sophisticated equipment is necessary
- **Disadvantages:** larger incisions, increased post-operative complications

Extracapsular cataract extraction (ECCE)

- This involves extraction of the lens through an opening in the anterior capsule whilst leaving the posterior capsule.
- The intact posterior capsule anchors the artificial lens.
- Advantages: better anatomical placement of the artificial lens, smaller incisions, decreased post-operative complications

- Disadvantages: a requirement is that the zonule ligaments must be intact and provide adequate support

The lens can be removed: manually (standard ECCE)

- By ultrasound driven needle to fragment and then aspirate the lens (phaeco-emulsification)

Clinical notes

- Cataracts may be seen easily with the unaided eye.
- This should make the diagnosis straightforward.
- **Large dense cataracts will cause a white pupil.**
- Examining the red reflex is important.
- With **small cataracts**, the, **red reflex will be reduced**
- In **larger dense cataracts**, the **red reflex will be absent**
- This examination technique can be applied to small cataracts, in which there is some degree of red reflex (as opposed to a total loss).
- When **examining the red reflex with +4 dioptres** at approximately **20cm from the eye**, the cataract will manifest as a **black opacity surrounded by the red tinge of the reflex**.
- Ask the patient to look up.
- If it **moves up on upward gaze**; then it 'is **located** in the **anterior half of the lens** (**anterior capsular cataracts**).
- **If it moves down on upward gaze**, then it is located in the **posterior half of the lens (posterior capsular cataracts).**
- The position of **cataracts located in the centre** (**nuclear** cataracts) **will not be affected**.
- **This simple manoeuvre helps localize cataracts**, and will impress examiners.

Causes of Cataract:

a. **Senile cataracts:** patient age; **arcus senilis**
b. **Diabetes:** diabetic fingertip **skin pricks** (glucose testing); features of **diabetic retinopathy** in unaffected eye
c. **Cushing's syndrome:** moon face; centripetal obesity; buffalo hump; striae; purpura; proximal myopathy
d. **Myotonic dystrophy:** frontal balding; temporalis wasting; partial ptosis
e. **Hypoparathyroidism:** Chvostek's and Trousseau's signs
f. **Bardet-Biedl syndrome:** retinal pigmentation; polydactyly, short stature; truncal obesity
g. **Refsum's disease:** peripheral neuropathy, nystagmus; cerebellar signs, hearing aid (deafness); ichthyosis
h. **Homocystinuria:** marfanoid habitus; downward lens dislocation; livedo reticularis
i. **Turner's syndrome:** short stature; webbed neck; cubitus valgus; widely' spaced nipples; high arch palate
j. **Down's syndrome:** round face; epicanthic folds; flat occiput; protruding tongue; single palmar crease; 5th finger clinodactyly; wide sandal gap

k. **Fabry's disease:** arthropathy; angiokeratoma; restrictive cardiomyopathy
l. **Wilson's disease:** tremor; chorea; dysarthria (akinetic rigid syndrome); arthropathy; features of **chronic liver disease**
m. **Drugs**

MRCP-PACES

Brief Clinical Consultation

Charcot's joint

You are a doctor in the diabetes clinic.
Mr. Edwardo is 36 years old, male
Has been referred by his GP with difficulty of walking
Your task: to assess the patient's problems and address any questions or concerns raised by him

Confirmations:

- Self
- Patient
- Agenda

Opening question - background:

- I received a letter from your GP mentioning that you have difficulty of walking
- Could you tell me more about that?
    - I have difficulty with my ankle when I try to get round the house

Brief analysis of ankle difficulty:

- **What do you mean exactly by difficulty with your ankle?**
    - It is getting swollen
- **In which joint you have problem?**
- **Do you have problem in any other joint?**
- **Any pain, redness, or problem with movement of your ankle?**
- **ODPARA**
    - ✓ Onset – sudden or gradual
    - ✓ For how long
    - ✓ Is it the same improving or worsening?
- **Can I have A look?**

- **Joint:**
    - Any joint enlargement?
    - Any joint change like:
        - Instability
        - Hypermobility
        - Getting warmer
    - Pain?
    - Crepitus or crackling
    - Deformity?
    - Skin change
- **Osteomyelitis:**
    - **Any trauma?**
    - Any fall?
    - Any discharge?
    - Any high body temperature?
- **Vascular insufficiency:**
    - Any ulcers on the feet or toes?
    - Any pain in legs or calves while walking?
    - Any rest pains?
- **Neuropathy:**
    - Any loss of sensation?
    - Any abnormal sensation?
    - What do you mean by abnormal sensation – numbness, pins, etc.
    - Any **numbness**, burning, pain, paranesthesia
        - Up to where in your legs.
    - Any changes in walking – high steppage gait
    - **Any unsteadiness**
    - Any falls
    - Any weakness
    - What nature? – flobby or stiffy
- **Causes of neuropathy:**
    - What about your diet?
        - vitamin B12 and folate
    - Do you take alcohol
    - Any lumps or pumps - paraneoplastic

- Any weather preference,
- neck swelling? - hypothyroidism

Past Medical history:

- Any medical condition you have I should be aware of?
  - I have DM
- How long has he had diabetes?
- Is it controlled?
- **What was the last 3 months blood sugar reading?**
- Are you monitoring the blood sugars?
- What medications you are taking?
- Over how long you are being on them?
  - I have not been taking medications for several months because of the 'hypo' episodes which I frequently had when taking them
- What is the usual range for blood sugar readings?
- Are you following regularly with the eye doctor?
- Are you checking your kidney function?
- Any changes in his weight over the past 6 months?
- Are you talking a balanced diet?
- Are you following with chiropodist for food care?
- Are you exercising?
- **Complications of DM:**
  - Any change in eyesight?
  - Any chest pains?
  - Any change in water work?
  - Any weakness anywhere?
- Any history of high BP?
- Are you checking the BP?
- Any history of high Cholesterol?

Family history:

Drug history:

Social history:

- What you do for living?
- Any help needed?
- How is the home condition?

- In which floor you are living?
- Any rails or support fixed in bedroom and bathroom
- How have you managed shopping?
- With whom you are living?
- How these symptoms affect you with daily activity?
- Smoking
- Alcohol
- **Driving - stop for recurrent `hypos'**
- **Also stop if unaware about hypos**

Can I examine you?

- **Examine the affected joint:**
    - Inspection of the affected limb – loss of digits, amputation
    - Charcot joint is painless, deformed and swollen, with an abnormal range of movement
    - Check active and passive ranges of movement
    - Probably restricted joint instability
    - hypermobility of the joint
    - Crepitus will be marked, but you should not test for it!
- **Skin:**
    - Dryness
    - Hairless skin
    - Check temperature by dorsum of your hand
    - Look for ulcers and callus on the feet
- **Assess vascular supply to the feet**
    - Pulses in the popliteal, dorsalis pedis and posterior tibial arteries
    - Assess capillary refill
- **I would like to carry out a full neurological examination of lower limbs**
    - Look for muscle wasting across the affected joint - compare with other side
    - Tone, power, and reflexes around the joint
    - Loss- reduction in Achilles tendon reflex
    - **Test sensation:**
        - Cotton piece - close eye as soon as feel tell me

        - Loss of light touch, **proprioception**, joint position, and vibration - use a 128Hz tuning fork – posterior column signs
        - Loss of pain, fine touch, temperature
        - **Joint position**
- **Look for signs of the other causes of Charcot joint:**
    - **Syringomyelia**- dissociated sensory loss
    - **Tabes dorsalis** – neurosyphilis
        - Ulcers on the fee
        - Argyll-Robertson pupils
    - **Paraplegia**
    - **Leprosy**
    - **Myelomeningocele**
    - **Hereditary sensory neuropathies**
    - **Congenital insensitivity to pain**
- **Assessing gait:**
    - **Looking for ataxia**
    - High-stepping gait - loss of proprioception in the ankle
    - **Positive Romberg's sign**
- **I would like to complete my examination by**
    - Examining the upper limb for neurology
    - Check blood sugar checking marks in finger pulps
    - Check BP, sitting, standing
    - Check urine for sugar and proteins
    - Doing fundoscopy

What is your concern?

- **What is wrong with me?**
- From what you told me and after I examined you, most likely you have a condition called Charcot's Joint in which the nerves in your legs have been affected by your diabetes
- Your ankle has been damaged by this as well, as you have not been able to feel when it has been injured, and this looks to have led to chronic joint damage
- We will need to do blood tests to exclude other causes of the nerve problems, and involve a group of professionals to help you with your diabetes and your ankle problems

- This will include the diabetes team, podiatrists, **orthotists**, and orthopedic surgeons
- We will need to check you are up to date with your eye and kidney checks too.
- It is important that you control your blood sugars as strictly as possible to reduce the risk of further damage to your body from the diabetes

Why has the diabetes damaged my joints?

- The diabetes has affected the nerves in your legs so that they are less sensitive.
- You have not, therefore, noticed when you suffered an injury to your ankle, and the damage to your ankle has continued up until now without you realizing.
- Your ankle joint is now severely damaged
  and we need a team of specialists to help you with this

Will I need an operation?

- The damage to the ankle joint is usually treated initially with a cast or boot to protect the foot and ankle, followed by custom-made shoes, rather than an operation
- It is important to protect the feet as you will be at risk of developing foot ulcers due to the loss of feeling in the feet and the ankle joint.
- Sometimes operations are needed if the instability of your ankle puts you at too high a risk of ulceration or the footwear is ineffective
- Surgery does, however, carry a significant risk of infection and other problems due to the damage to the bone and the soft tissue around the joint in conjunction with your diabetes

Is it reversible?

- Mostly not

Examiners' questions:

What are your findings?

- **On examination of this gentleman:**
- The **skin** has a **shiny** and **dry** appearance with **loss of hair** up to the mid-calves.
- There are **ulcer** and **callosities** present on the soles of the feet
- The **ankle joints are swollen and deformed**, with **abnormal range** of **movements**

- There is **distal wasting** of muscles of lower limbs
- There is loss of vibration sense, light touch, and joint position
- Loss of pain and temperature in stocking distribution up to knees
- **Absent peripheral pulses** - NB: in the predominantly neuropathic foot the pulses may be present or even bounding, and the veins may be prominent (Ward's sign).
- **Positive Romberg's sign**
- Loss of digits - amputation

What is your diagnosis?

- Charcot's joint

What do you understand by the term Charcot's joint?

- It is a chronic progressive degenerative neuropathic arthropathy resulting from a disturbance in the sensory innervation of the affected joint.
- It results in gross deformity, osteoarthrosis, and new bone formation from repeated trauma.
- It is a complication of various disorders affecting the nervous system.

What are the differential diagnoses of deformity?

1. **Charcot's joint**
2. **Osteomyelitis**
3. **Trauma**

What is the cause of peripheral neuropathy in this case?

1. DM
2. Alcohol
3. B12 deficiency

How you will investigate this case?

- **Basic investigations:**
    - **Inflammatory markers**
    - **CBC** - WBC
    - **LFT** - alcoholism
    - **Electrolytes**
        - Calcium phosphorus, and alkaline phosphatase - bone metastasis, Paget's disease
    - **PTH**
    - **RFT**

- **Urinalysis:**
    - Sugar
    - Protein
    - Albumin: creatinine ratio
- Fasting blood glucose
- HbA1c
- **Thyroid function test**
- **Vitamin B12 and folate**
- ANA
- Autoimmune screen
- Protein electrophoresis
- Bence Jones protein
- VDRL/TPHA – syphilis serology
- **Nerve conduction study**
- X Ray ankle
- **MRI ankle:**
    - May help distinguish between **osteomyelitis** and Charcot arthropathy.
- **Bone scanning:**
    - Not always ordered may help differentiate between Charcot arthropathy and osteomyelitis.
    - An **indium-111 WBC scan** often is used because it is more specific than the technetium-99m scan
- **Doppler US** to rule out DVT

How you manage this case?

- **Patient education and counseling**
    - The total healing process typically takes 1-2 years.
    - Preventing further injury, noting temperature changes, checking feet every day, reporting trauma, and receiving professional foot care also are important tenets of treatment
    - **If diabetic:**
        - If you take care of your feet, you can avoid many complications
        - Daily **inspect your feet**, including your sloe by a mirror.

        - Daily **wash your feet and dry them** gently but not to rub.
        - Do **not walk bare foot** and wear **comfortable shoes** and socks
        - Get **regular visits for your feet care**.
        - If you get any wound, **immediately visit the doctor**.
    - **Referrals depend on the underlying problems in Diabetes Mellitus and include the followings**
        - General Physician
        - Diabetes specialist
        - Diabetes Foot clinic
        - Clinical nurse specialist
        - Foot Surgeon
        - Dietitian
        - Physical trainer
        - Physiotherapist
        - Blood channels surgeon
        - Eye specialist
        - Kidney specialist
        - Occupational health physician
- **Treatment mainly medical, non-operative approach:**
- **MDT approach**
    - **Diabetes specialist**
    - **Podiatry**, care with nail cutting
    - **Orthotist**
- **Immobilization:**
    - Cast to immobilize
    - Reduction in weight-bearing for prolonged periods, e.g. **3–6 months in a cast**
    - **Braces**
    - **Custom foot wears - Ankle-foot orthoses**
- **Foot care:**
    - Avoid injuries
    - **Avoid weight bearing**
    - Management of diabetic neuropathy

- Tight control of diabetes

- **Another therapy that is currently being researched are:**
  - **Low-intensity ultrasound**
  - **Electrical stimulation** and **magnetic field therapy** to stimulate bone formation.

  - The use of bisphosphonates to treat acute Charcot arthropathy is not warranted, unless as part of a clinical trial.

- **Surgery:**
  - Is indicated for **misaligned**, **unstable**, or **nonreducible fractures or dislocations**, as well as for cases in which **nonsurgical means fail**

  - The major contraindication for surgery is active inflammation

What is the prognosis?

- The prognosis depends mainly upon early recognition of the problem and effective management which includes patient education, diabetes control and MDT foot clinics
- A more favorable outcome is elicited when joints are treated within 2 weeks of injury and when there is strict adherence to weightbearing precautions

Mention a few conditions responsible for the development of Charcot's joints

- **Diabetic neuropathy**
- **Alcohol**
- **Tabes dorsalis:**
  - Affecting knee, hip, ankle, lumbar and lower dorsal vertebrae
- Cerebral Palsy
- **Syringomyelia:**
  - Affecting shoulder, elbow, cervical vertebra
- **Myelomeningocele**
- Hereditary sensory neuropathies
- Peripheral nerve injury
- Congenital insensitivity to pain
- **Leprosy**

- **Paraplegia** (hips)
- **Neurofibromatosis**
- **Porphyria**

What are the causes of peripheral neuropathy?

- DM
- Alcohol

What is the advantage of measuring skin temperature in Charcot's foot?

- Skin temperature difference between feet, measured with a contact or non-contact thermometer, may be significant.
- The average difference between the acute Charcot's foot and the unaffected side is as much as 9°F (5°C).
- A difference of 4°F (2°C) is considered significant.

How is Charcot's foot classified?

- The Rogers and Bevilacqua classification combine the features of the clinical examination, radiography, and anatomy.
- There is increasing risk for amputation as the Charcot foot becomes 'more complicated'

What are the 6Ps of prevention of neuropathic foot?

1. Podiatry
2. Pulse examination
3. Protective shoes
4. Pressure reduction
5. Prophylactic surgery
6. Preventive education

What are the complications of Charcot's arthropathy?

- Fracture
- Deformity
- Infection
- Amputation

MRCP-PACES

Brief Clinical Consultation

Chest pain

Role: On-call medical registrar
Mr. Edwardu is **34 years old male**, has been admitted to the ward with fever and breathlessness.
He has a history of HIV diagnosed 3 years ago and has not previously been on retroviral therapy.
He has been treated for pneumocystis jiroveci pneumonia (PCP) with high dose cotrimoxazole.
He had improved cons1derably and his supplementary oxygen requirements had reduced considerably, with oxygen saturations of 96% on room air
This morning whilst mobilizing from his bed to the toilet he developed sudden onset of left –sided chest pain and breathlessness.
He is a smoker and has a strong family history of ischaemic heart disease.
Routine observations taken by the ward sister demonstrate a heart rate of I 02 beats per minute
His blood pressure was 138/78 mmHg, oxygen saturations of 90% on room air.
She has requested an urgent medical registrar review.
Task. Assess the patient and advise on further investigations and treatment

Confirmations:

- Self
- Patient
- Agenda

Check:

- Expectations
- Knowledge
- How she feels

Opening question:

- I got to know that you have been troubled with chest pain
- Could you tell me more about that?
- I have been admitted with high body temperature and SOB and have been diagnosed with a specific bug infection in chest which the doctor term as PCP.
- I have now been on through needle antimicrobial therapy for I week and have improved considerably.
- I am no longer requiring supplementary oxygen.
- This afternoon, whilst getting up from the bed to go the toilet I develop severe left-sided chest pain with associated SOB.

Empathy and sympathy:

History of presenting complaint

- How long have the symptoms been present for?
- **What are the characteristics of the chest pain?**
    - Onset? (Gradual or sudden)
    - Nature? (Dull, sharp or burning)
        - It is sharp in nature and increased by movement and deep inspiration.
    - Location?
    - Radiation?
        - There is no radiation.
- **Exacerbating and relieving factors:**
    - Exertion?
    - Deep breathing? (Pleuritic)
    - Hunger?
    - Eating?
    - Posture, i.e. lying down or sitting up? (Lying down can increase discomfort in gastro-esophageal reflux and Pericarditis)
- **Are there any associated symptoms?**
    - SOB?
    - Heart racing?
    - Feeling sick and sweating?
    - Tummy pain?
    - Acid taste in mouth?
    - Cough, phlegm, or coughing up blood
    - There is no calf pain, swelling or tenderness.

PMH:

- You have been diagnosed with HIV 3 years ago following health insurance screening tests.
- Besides HIV you have no other significant medical history.
- Ischaemic heart disease.
- Enquire about cardiovascular risk factors
- A recent MI can result in Pericarditis (Dressler's syndrome)-this is associated with pleuritic chest pain
- Chronic respiratory disease
- Pneumothorax
- Thromboembolic disease
- Thrombophilia

Drug history:

- I do not take regular medications and there are no allergies.
- Review patient's drug chart
- Has the patient been prescribed DVT prophylaxis?
- Is the patient on retroviral therapy?
- Is the patient on pentamidine prophylaxis?
    - Pentamidine prophylaxis increases the risk of PCP associated pneumothorax.

Social History:

- Smoker and smoke up to 20 cigarettes per day.
    - Smoking increases the risk of pneumothorax
- You drink minimal alcohol

Family History:

- Strong family history of coronary artery disease with both brother suffering heart attacks aged 55 and 51 years.
- Thrombophilia

Can I examine you?

- Review **observation chart**
- Check **heart rate** and **blood pressure**
- **Respiratory rate** and **oxygen saturations**
- **Examine chest**
    - **Musculoskeletal chest pain**:
        - Palpate for chest wall tenderness
        - Look for evidence of chest trauma
- **Pneumothorax**:
    - Tracheal deviation to the opposite side
    - Ipsilateral reduction in chest expansion
    - Hyper-resonance
    - Reduction in breath sounds
- **PE**:
    - Often no signs
- **Pleural rub**
- **Features of consolidation**
- **Examine heart**
    - Features of **pulmonary hypertension**:
        - Raised JVP
        - Parasternal heave
        - Loud P2
    - Pericardial rub - Pericarditis is a cause of pleuritic chest pain, but will not explain the hypoxia
- **Examine legs**
    - Calf swelling and tenderness

What is your concern?

(a) Am I having a heart attack?
(b) If not what is it?
(c) Will I need more tests?

- My current symptoms resemble that of my brothers' symptoms when they had heart attacks.
- Given the strong family history I am concerned that I may be having a heart attack.

- I highly respect your worries, from what you told me and after I examined you, although the cause of chest pain is not clear but heart attack is less likely
- The characteristics of the chest pain do not suggest a heart attack.
- However a heart tracing will be requested.

- Initially, it is important to exclude air surrounding covering layers of your lung and you will arrange a chest X-ray to look for this.
- The type of bug infection you have increases this risk
- If the chest X-ray does not show air surrounding covering layers of your lung, then one must consider the possibility of clot in major blood channels in lung.
- A clot in the lung can occur in patients who are hospitalized as immobility is a risk factor
- This can be diagnosed using a chest scan
- The oxygen levels in the blood are low, and this warrants supplementary oxygen.
- Analgesia can be given to control the pain.
- The specific treatment depends on what these investigations will show and the exact cause
- Is that okay with you?

Questions commonly asked by examiners

What are the differential diagnoses of pleuritic chest pain and hypoxia?

(a) PE
(b) Pneumothorax (complication of PCP)

How you will investigate this case?

- **Arterial blood gas**
- **ECG**
- **CXR**
- Request a (PA) film to look for pneumothorax
- If the clinical suspicion of a pneumothorax is high, but the PA chest radiograph is normal, a lateral chest or lateral decubitus film should be requested.
- A CXR can also demonstrate other causes of pleuritic chest pain i.e. consolidation or collapse
- **CT pulmonary angiogram** (if clinical suspicion of PE)
- **Doppler ultrasound** of leg (if clinical suspicion of DVT)

How you will manage this case?

- **Oxygen**
- **Analgesia**
- If CXR confirms pneumothorax, then aspiration +/- intercostal drain
- If CXR does not show a pneumothorax, then anticoagulate with low molecular weight
- heparin and request CT pulmonary angiogram to look for PE
- If CT pulmonary angiogram does not show a PE then consider other **causes of pleuritic chest pain:**
  - **(a) Pleurisy**
  - **(b) Pericarditis**
  - **(c) Musculoskeletal chest pain**
- The hypoxia in the above case is against these diagnoses.
- However, the hypoxia may be a manifestation of PCP.

- It is important to remember that in extreme cases, severe pleuritic chest pain can result in voluntary splinting of the chest and hypoventilation, which can lead to hypoxia.
- In such cases, adequate analgesia is helpful-both therapeutically and diagnostically.
- **Other issues to address:**
- Check CD4 count and initiate anti-retroviral therapy (highly active anti-retroviral therapy HAART)
- PCP prophylaxis (pentamidine)

What is the differential diagnosis of pleuritic chest pain?

(a) Pulmonary embolism
(b) Pneumonia
(c) Malignancy
(d) Pleurisy
(e) Pneumothorax
(f) Musculoskeletal chest pain
(g) Pericarditis

What ECG changes are seen in Pericarditis?

- Global saddle shaped ST segment elevation
- PR segment depression

What are the causes of Pericarditis?

- **Viral infections**
    - coxsackie
    - adenovirus
    - echovirus
- **Bacterial infections**
    - Mycoplasma
    - Haemophilus
    - tuberculosis
- **Connective tissue disease**
    - rheumatoid arthritis
    - SLE
- **Drugs**
    - Hydralazine
    - Procainamide
- **Dressler's syndrome**
    - post myocardial infarction
    - cardiac surgery
- **Uremia**

What are the risk factors for PCP-associated pneumothorax?'

- Smoking
- History of pentamidine chemoprophylaxis
- Pneumatoceles identified on CXR

- The history of pleuritic chest pain is clear, and this is against a diagnosis of cardiac ischemia.
- Therefore, the patient can be reassured.
- In the absence of clinical signs of pneumothorax, the most likely diagnosis is a PE.

- PE should be considered in hospitalized patients who may be relatively immobile.
- PCP-associated pneumothorax is seen in approximately 5% of patients with PCP, and thus pneumothorax must be considered in the differential diagnosis for this patient.
- A pneumothorax must be excluded prior to commencing anticoagulation for PE as this may warrant aspiration +/- intercostal drain insertion.

MRCP-PACES

Brief Clinical Consultation

Cushing's syndrome

Scenario:

- You are SHO in the clinic
- Miss. Lara, complaining of **menstrual irregularity**
- Another possible scenario:
  - You are the registrar in endocrinology clinic.
  - A 65-year-old woman has been referred by her GP with concerns relating to weight gain.
  - She is well known to the respiratory service with chronic restrictive airways disease but recently missed her annual review, although she was seen in the cardiology clinic 1-month prior.
  - Please obtain a history, an examination is not required, and discuss your thoughts with the patient including plans for further investigation or management.

Confirmations:

- Self
- Patient
- Agenda

Opening question:

- 'I understand that you are normally reviewed in the respiratory clinic, and recently you started to get changes in your period, can you tell me more about that'.

Analysis of menstrual irregularity:

ODPAR-OCD

- What do you mean exactly by menstrual irregularity?
- When was your last period?
- Is it scanty?

- Is it on and off? I mean some months coming and stop on others?
- What is the amount exactly?
- Is it less in number of days compared to before?
- May I ask you a private question if you allow me?
- Do you have a partner?
- Do you use any birth control pills?
- Any chance of pregnancy?
- What about your intimate relationship? - **loss of libido**

Screen more for the cause of menstrual irregularity:

- **Any weight gains?**
  - Yes
- How much you gained and over how long time?
- Is it **intentional**?
- What about your appetite?
- In which part of your part did you gain weight more?
  - In my tummy?
- **Association of weight changes:**
  - **OSA** - Any snoring or daytime sleepiness and headache?
  - **Carpal Tunnel syndrome** – in pain in hand, any pain if I tap here?

Screen for differential diagnosis of weight gain:

- **Cushing's syndrome**
  - Any thin skin with stretch marks, acne, hyperpigmentation
    - Yes, I am getting **bruises** in my tummy
    - Poor wound healing
    - **Consider causes of easy bruising.**
      - Is the patient on any medications which would put her at higher risk such as anti-platelet agents?
      - Has the patient had any active bleeding such as epistaxis?
  - Change in facial appearance
  - Difficulty of combing hair or raising up from a chair
- **Polycystic ovary syndrome**
  - Abnormal hair growth - Hirsutism,
  - Any skin rash – acne?
  - Any in history of difficulty of getting pregnancy?

- Obesity, irregular menses, diabetes
- **Hypothyroidism -** Cold intolerance, Generalized fatigue, Mood changes, tiredness and lethargy, weakness, cold intolerance, anorexia, dry skin, constipation, menorrhagia
- **DM -** Increased appetite, are you passing more urine than usual or drinking more than usual?
- **Insulinoma -** Fainting attacks, sweating, low glucose level measures before food
- **Salt and water retention:**
  - **CLD**- yellow discoloration, tummy pain
  - **CKD**- change in water work
  - **Nephrotic syndrome** – frothy urine – water work, morning puffy eye lids
  - **Hypoalbuminemia**- leg swelling, diet, appetite
  - **Congestive heart failure** – SOB, leg swelling, chest pain, difficulty of berating with exertion or laying down
  - **Increased intake with reduced exercise**
  - **Pregnancy** – amenorrhoea, nausea, urinary frequency, breast tenderness

Screen for Cushing's syndrome complications:

- Difficulty rising from seated position - proximal myopathy
- Back pain – vertebral fracture from osteoporosis - osteopenia
- DM, HPN - Did you check your glucose level or BP before – controlled or not?
- **Recurrent skin infections**
- **Mental disturbance** including **low mood and depression**

  - Despite the likelihood of an iatrogenic cause, consider signs and symptoms that might suggest a **pituitary adenoma** including headaches and visual disturbance which is classically a **bitemporal hemianopia**.
  - **Polyuria** and **galactorrhoea** may also be seen.

Screen for the cause of Cushing's syndrome:

- **Exogenous**: signs of chronic condition (e.g. RA, COPD) requiring steroids
- **Endogenous**: bitemporal hemianopia and hyperpigmentation (if ACTH ↑), **increased intra-cranial pressure**

Past medical history:

- D.M
- HTN
- Cardiac problem
- Surgical operations

Family history:

- Similar problem or other medical disease

Drug history:

- Any drug intake like steroids or OCP - factitious Cushing
- Exogenous vs endogenous steroid

Social history:

- What is your job?
- How much these symptoms impact on your job & daily activity?
    - I will refer you to a social worker
- With whom are you living with?
- Any financial support needed?
- Smoking
- **Alcohol – pseudo-Cushing's**

Can I examination you?

- **Eye:**
    - Examine the visual fields for a **bitemporal hemianopia**
    - Tell the examiner you would like to examine the fundus for **optic atrophy**, **papilledema**, signs of **hypertensive or diabetic retinopathy**
- **Head**:
    - Round and plethoric face
    - Acne
    - Buccal mucosa fungal infection.
- **Body**:
    - **Face**: Round (moon-shaped), hirsute, with acne
    - **Supraclavicular and interscapular fat pad - avoid using the term 'buffalo hump'**
    - **Skin**
        - Thin skin – dorsum of hands

- Striae alba and rubra - purple striae – hyperpigmented
- Easy bruising
- **Hirsutism** - not common in Cushing syndrome caused by exogenous steroids because they suppress adrenal androgen secretion.

- **Chest**- signs pointing towards an underlying respiratory diagnosis necessitating long-term steroid therapy include:
  - Barrel chest with wheeze on auscultation (in the young patient, think of difficult-to-control asthma, whereas in the older patient be mindful of COPD)
  - If the patient has fine, end-inspiratory crepitations, think of fibrosis
  - Scars, such as those related to a lung transplant
- **Abdomen:**
  - Centripetal obesity
  - Thinning of skin and purple striae (also seen over the shoulders and thighs): said to be present on almost all patients
- **Legs:**
  - Wasting (‘lemon on sticks’ body shape)
  - Edema
  - Bruising
  - Weakness of the muscles of the shoulders and hips: get the patient to squat (proximal myopathy)
- **Complications**
  - **Hypertension** - Ask the examiner to measure BP
  - **Diabetes mellitus** - random blood glucose, Diabetic Dermopathy, Necrobiosis Lipoidica, Peripheral Neuropathy
  - **Osteoporosis** – kyphosis, palpation the back for tenderness
  - **Cellulitis**
  - **Proximal myopathy** - stand from sitting position with folded arms to chest

In case of Iatrogenic Cushing’s syndrome:

- **Examine for the cause if drug induced:**

- **Sarcoidosis** (examine chest for fibrosis, lupus pernio, HSM)
- **SLE** (examine chest for lung fibrosis, pleural effusion, butterfly rash, joint pains)
- **Polymyositis** (proximal weakness)
- **Dermatomyositis** (Proximal Muscle Weakness, Heliotrope Rash, Gottron's Papules)
- **Transplanted Kidney**
    - Signs of Immunosuppression, iliac fossa scar
    - Previous hemodialysis signs
    - Palpable dull mass under the scar
- **COPD Signs.**

What is concern?

What is wrong with me doctor?

I am so concerned about my appearance

- 'From our consultation today, I suspect you have a condition called Cushing's syndrome which is when there is too much protein in your body, called steroid hormone
- Most likely it is caused by the steroid used to treat your lung scaring - fibrosis.
- This is likely what has caused your period irregularity, weight gain and easy bruising which you have
- I would like to arrange for some tests to confirm the diagnosis.
- It will be important to get the input of the lung doctor in adjusting your medication and consider alternative management options and will refer you to gland doctor and social worker for better plan of care'
- **Is that okay with you?**
- **Do you have any other concern?**

'The GP mentioned the possibility of side effects from steroids but was reluctant to change my medication due to the nature and severity of the fibrosis and current breathlessness:

'Does this mean I need to stop steroids, and if so, how will that impact upon my fibrosis?'

'If I stop the steroid, will the weight gain be reversible, or can I expect symptoms to continue to get worse?'

Examiners' questions:

What are your findings?

- 'This patient has a **Cushingoid appearance** consistent with steroid excess.'

What is your diagnosis?

- 'This patient has signs consistent with a diagnosis of Cushing's syndrome, which is likely iatrogenic and secondary to their underlying respiratory disease.'

What are your differential diagnoses?

1. ACTH-secreting pituitary adenoma - **Cushing's disease**
2. Excess endogenous steroid from an adrenal adenoma - **Cushing's syndrome**
3. **Pseudo-Cushing's** from conditions such as **depression** and **alcohol** excess - absence of signs of **chronic liver disease.**
4. **Exogenous steroid use**
    - Differential of **underlying respiratory diseases** which warrant steroid therapy and are therefore prone to **iatrogenic Cushing's,** such as:

    i. Asthma
    ii. COPD
    iii. Fibrosis
    iv. Lung transplantation

How you will investigate this case?

Basic Investigations:

- Full blood count
- renal function and electrolytes – **hypokalemia**
- liver function
- glucose
- lipids
- HbA1c
- baseline cortisol
- pituitary function
- **Urine dipstick** can be useful in assessing for glycosuria

Investigate the underlying respiratory diagnosis - iatrogenic steroid:

- **A plain chest radiographs**
  - ✓ **hyperexpanded lung fields** in **COPD** and difficult to- control **asthma**
  - ✓ **reticulonodular shadowing** if the underlying disease process is pulmonary **fibrosis**
- **Peak expiratory flow rate**

Confirm Cushing's syndrome:

► Tests to confirm the diagnosis of hypercortisolism:

- **Urinary free cortisol as 24-h collection**:
  - This is the most direct and **reliable practical** index of cortisol secretion.
  - The reason is that plasma concentrations of ACTH and cortisol fall and rise episodically, in normal subjects, in Cushing syndrome and in ectopic ACTH syndrome
  - If urinary free cortisol elevated and failed overnight dexamethasone suppression test, confirm the diagnosis with low dose dexamethasone suppression
- **Measurement** of **midnight salivary cortisol levels**
- **Overnight dexamethasone test**
- **Plasma cortisol.**
  - ✓ **High-dose dexamethasone suppression test** may help >50% suppressed cortisol: Cushing's disease
  - ✓ **Suppressed cortisol**: alcohol/depression/obesity ('pseudo-Cushing's')

► Tests to determine the site of hormone production:

- **Low-and high-dose dexamethasone test:**
  - **low-dose dexamethasone fails to suppress urinary steroid secretion** in **Cushing's disease** whereas **high dose dexamethasone** (2 mg every 6 h for 2 days) **suppresses at least** 50**% of urinary steroid secretion**
  - Low dose dexamethasone suppression testing demonstrates a failure to suppress cortisol levels
  - Where the low dose dexamethasone test is positive ACTH is measured. ACTH levels will be undetectable in primary adrenal disorders, whereas ACTH will be high if

the cause is either Cushing's disease or an ectopic ACTH producing tumor
        - Where the low dose dexamethasone test is positive and the ACTH is raised, performing a 48-hour dexamethasone test will confirm Cushing's disease as evidenced by a partial suppression of cortisol. Imaging will then be required with CT or MRI brain for pituitary disease
- **Chest radiography** for carcinoma of the bronchus
- **Plain radiograph of the abdomen** for **adrenal calcification**
- **Ultrasonography of the abdomen for adrenal tumors**
- **If Cushing's disease is suspected:**
    - **ACTH level**
        - Assess whether is **ACTH dependent** or **independent** with serum ACTH value
        - A high dose dexamethasone suppression tests differentiates pituitary ACTH from ectopic ACTH production
        - **High**: ectopic **ACTH secreting tumor** or **pituitary adenoma**
        - **Low: adrenal adenoma/carcinoma**
        - **plasma ACTH:** >10 pg per mL (2 pmol per L) suggests ACTH dependency; a level below 5 p/l (1 pmol/l) suggests an adrenal source
    - **Radiography of pituitary**
        - **MRI gadolinium enhancement**: MRI can identify pituitary tumors approximately 60% of the time once ACTH dependency is established
    - **Bilateral measurement of ACTH in the inferior petrosal sinus;** Cushing's disease is the most likely diagnosis if the sinus-to-peripheral vein ratio of plasma ACTH is at least 2:1 before or at least 3:1 after injection of ACTH-releasing hormone (corticotrophin-releasing hormone (CRH)) during sampling from the inferior petrosal sinus
    - **CRH test** (helpful in distinguishing pituitary-led Cushing's disease from ectopic ACTH secretion)

- Inferior petrosal sinus sampling is used to distinguish primary and ectopic sources of ACTH when the source of the ACTH is not obvious based on clinical circumstances, biochemical evaluation, and imaging studies.
- **Bilateral inferior petrosal sinus vein sampling** (best test to confirm pituitary vs ectopic origin; may also lateralize pituitary adenoma)

How are you going to treat this case?

✓ **Treatment of underlying cause:**

- If the cause is found to be exposure to exogenous steroid, this should be stopped.
- **Management of iatrogenic Cushing's syndrome:**

¦ Reduce the need for steroid through use of steroid-sparing agents.
¦ Management of cardiovascular risk including screening for diabetes, good glycemic control in those with steroid-induced diabetes, addressing hypertension and lipid management.

✓ **Surgical**:

- **Trans-sphenoidal hyphesectomy** to remove pituitary tumors.
- **Adrenalectomy for adrenal tumors – adenoma**

  - **Nelson's syndrome**: **bilateral adrenalectomy** to treat **Cushing's disease**, can cause **massive production of ACTH** (and **melanocyte-stimulating hormone**), due to **lack** of **feedback inhibition**, leading to **hyper-pigmentation** and **pituitary overgrowth**

- **Pituitary irradiation**
- **Medical**:
  - **Metyrapone -** can be used to decrease plasma cortisol levels
  - **Ketoconazole**

What is cause of death in this case?

- **Untreated** Cushing's syndrome: **50% mortality at 5 years**
- Usually due to **accelerated ischemic heart disease** secondary to **diabetes** and **hypertension**

Pigmented abdominal striae are visible on the patient's abdomen.
The patient has central adiposity.
The infra-umbilical scar is also pigmented.

What are the medications that can cause weight increment?

- **Lithium** and **amiodarone** - hypothyroidism
- **Calcium channel blockers** - peripheral oedema
- **Steroids**
- **Anabolic steroids**
- **Growth hormone**
- **Anti-psychotics** - olanzapine - increases appetite

Mention some causes of Cushing syndrome

- **Steroids**, including **ACTH**
- **Pituitary adenoma** (**Cushing's disease**)
- **Adrenal adenoma**
- **Adrenal carcinoma**
- **Ectopic ACTH** (usually by small cell **carcinoma** of the **lung**): the presence of **hyperpigmentation or hypokalemic alkalosis** suggests that the Cushing syndrome results from ectopic ACTH secretion.

What is the difference between Cushing's disease and Cushing syndrome?

- **Cushing's disease** is **increased** production **by the adrenals secondary** to **excess pituitary ACTH**, whereas **Cushing syndrome** is caused by **excess steroid from any cause.**

What is pseudo-Cushing syndrome?

- In **chronic alcoholics** and patients with **depression**, there may be
  - **Increased urinary excretion of steroids**
  - **Absent diurnal variation of plasma steroids**
  - **Positive overnight dexamethasone test**.
- All these investigations return to normal on discontinuation of alcohol or improvement of emotional status.

What do you know about Nelson syndrome?

- It is a syndrome that occurs **after bilateral adrenalectomy** and is characterized by
  - **Rapidly growing pituitary adenoma**
  - **Extremely high ACTH levels**
  - **Hyperpigmentation**.
- As the incidence may be as high as 50%, **patients with Cushing's disease** who have **undergone adrenalectomy** should be **followed by regular plasma ACTH** levels and **imaging for pituitary tumors**.

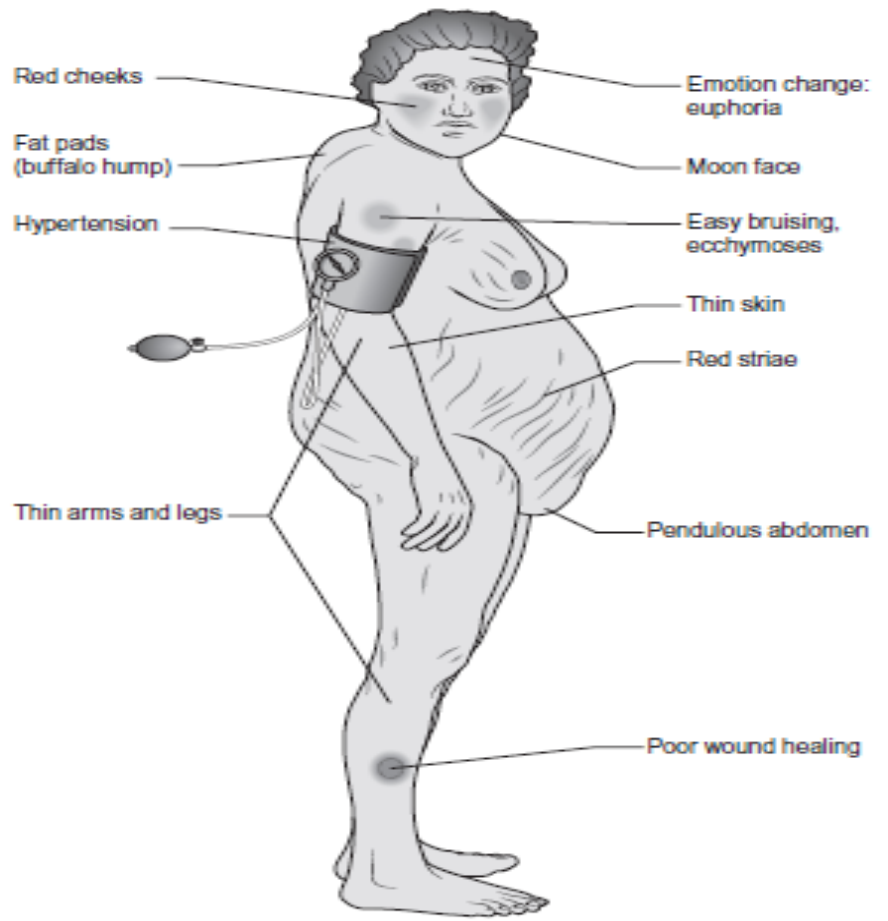


Fig. 145.1 Typical findings in Cushing syndrome.

MRCP-PACES

Brief Clinical Consultation

Cushing's syndrome

You are the SHO in the GIM unit
Miss. Suzan, 34 years old, with high blood pressure

Confirmations:

- Self
- Patient
- Agenda

Opening question:

- You got troubled with high blood pressure
- Could you tell me more about it?

Analysis of high blood pressure:

ODPARA

- Onset
- Duration
- When last time you checked your blood pressure
- Any headache?
- Any weight gain?
- Where did you put on weight more in your body?

Association:

- Any mood change?
- Any high blood sugar?
- Any skin changes?
    - Yes I have bruises in my tummy
- **Steroid-responsive conditions:**
    - **Asthma/COPD**: wheeze
    - **Interstitial lung disease**: SOB, cough
    - **Rheumatoid arthritis**: joint pain
    - **SLE**: rash in sun exposed skin
- **Ectopic ACTH secreting tumours:**
    - **Small cell carcinoma of lung**: high body temperature, weight loss
    - **Carcinoid tumour**
    - Loose stool
    - Hear racing
- **High blood pressure complications:**

- Weakness
- Loss of sensations
- Sight problems
- Chest pain
- Heart racing
- SOB
- Leg swelling
- Change in water work

Drug history:

- Allergies
- Medication list
- Any steroids

Past medical history:

- Any significant illnesses
- Any radiotherapy
- Any surgeries
- Fractures – thin bones

Family History:

- High blood pressure
- Malignancy

Social history:

- What is your job?
- QOL
- Smoking
- Alcohol

Can I examine you?

- Observation chart- BP, PR
- **Cushingoid facies**
- Centripetal obesity
- Interscapular and supra-clavicular fat pads.
- Acne vulgaris on the face and trunk
- Purpuric and petechial rashes consistent with bruising and thin skin.
- Violaceous striae on the abdomen
- Proximal myopathy.
- No adrenalectomy scars
- Lower limb edema
- CNS: weakness , sensory affection
- **Fundoscopy**
- Blood sugar checking markings

- Urine for blood sugar

What is your concern?

- **What's wrong with me?**
- From what you told me and after I examined you, most likely you have a condition called Cushing's syndrome, due to problem in glands overlying your kidneys secreting more protein called cortisol leading to many problems in your body, including skin changes, high blood pressure, high blood sugar , thinning of bones and others
- What we need to do is arrange some blood tests and imaging to confirm the diagnosis
- We will refer you to gland doctor for follow to follow you up and give you the best **anti-HTN medicine**
- Is that okay with you

What is your diagnosis?

- **Cushing's syndrome**

What is the management of Cushing's syndrome?

- The management of choice for endogenous Cushing's syndrome is **surgical resection of the causative tumour**, with **transphenoidal hypophysectomy** for Cushing's disease, and adrenalectomy for adrenal tumours.
- If surgery is unsuccessful or if symptoms require cortisol whilst waiting for surgery, medications that inhibit steroidogenesis may be used.
- **Ketoconazole** is the **first-line** agent used, **followed by** the addition of **metyrapone** if symptoms persist
- **Adjuvant radiotherapy** is used for Cushing's disease **if** transphenoidal **surgery is unsuccessful** or impossible.
- The **efficacy of radiotherapy is less than surgery**, and the **cortisol-lowering effect takes several months or years** so **anti-Adrenocortical medications** may also be required.
- **Adverse effects of radiotherapy** include **deficiency of other pituitary hormones, and cranial nerve palsies.**
- **Immediately following removal** of pituitary adrenal, or ectopic tumours, patients require **glucocorticoid replacement** at **'stress' doses**, which can be **slowly tapered**.
- **Bilateral adrenalectomy is only used for refractory cases** of Cushing's syndrome, where **surgery radiotherapy and medical therapy have failed**.

- These patients **require lifelong glucocorticoid** and **mineralocorticoid** replacement and are at **risk of Nelson's syndrome**.

Questions commonly asked by examiners

What do you understand by the terms 'Cushing's syndrome' and 'Cushing's disease'?

- Cushing's syndrome refers to the symptoms and signs caused by states of cortisol excess.
- Cushing's disease refers to hypersecretion of ACTH by a pituitary adenoma, which is one of the causes of Cushing's syndrome.
- Determining the cause of the excess cortisol require an understanding of the different types of Cushing's syndrome which may be ACTH-dependent or ACTH-independent.

ACTH-dependent Cushing's syndrome is **associated** with bilateral **adrenal hyperplasia**:

- **Cushing's disease** (ACTH hypersecretion by a pituitary adenoma)
- **Ectopic secretion of ACTH by a non-pituitary tumour** (small-cell lung tumors carcinoid tumours)

ACTH-independent Cushing's syndrome:

1. **Exogenous steroid administration** (iatrogenic or factitious Cushing's syndrome)
2. **Adrenocortical adenomas and carcinomas**

- The most common cause of Cushing's syndrome is exogenous steroid use.
- Ectopic ACTH syndrome occurs in 10% of patients with **small-cell lung tumours**, which is the **most common cause** of **ectopic ACTH secretion**.
- When it is **not iatrogenic**, i.e. due to exogenous steroid use, **Cushing's disease accounts for 80% of cases of Cushing's** syndrome
- **Ectopic ACTH production** accounts for 1**0%** (of which **half** are **benign** and **half malignant** ACTH sources), and **adrenal tumours account for 10%** (of which **half are benign** and **half malignant** ACTH sources).

How would you assess this patient?

History

- Ensure there is no history of **glucocorticoid use** including **oral, inhaled, and topical**.
- **Exclude pseudo-Cushing**, which is a state of cortisol excess complicating conditions such as **chronic infection**, **severe obesity, depression**, and **chronic alcoholism**.
- These patients have elevated cortisol levels, and may have some clinical features of Cushing's, but **do not develop the cutaneous manifestations or muscle weakness**.
- **Enquire about complications of Cushing's syndrome:**
    - **Diabetes** (polyuria and polydipsia)
    - **Osteoporosis** (back and bone pain)
    - **Avascular necrosis of femoral head** (restricted and painful hip movements)
    - **Proximal myopathy**
    - **Hypertension**
- **Demonstrate cortisol excess**
    - To determine cortisol excess, **random serum cortisol measurement is useless** since cortisol secretion is **pulsatile** throughout the day, even in Cushing's syndrome.
    - **24 hour urinary free cortisol** is a **reliable** method of demonstrating cortisol excess.
    - The test is typically **repeated three times**, since **three normal values exclude endogenous Cushing's syndrome**.
    - A value greater than three times the upper limit of normal is suggestive of Cushing's syndrome.
    - Mildly elevated values may represent Cushing's syndrome or pseudo-Cushing's, and require further assessment.
    - **Midnight serum cortisol** is an alternative **screening** tool for Cushing's syndrome, since the nocturnal **nadir** of serum cortisol is preserved in **physiological states** of cortisol excess, but the midnight cortisol is **elevated in Cushing's** syndrome.
    - However; this test does **not reliably distinguish Cushing's from pseudo-Cushing states.**
- **Dexamethasone suppression tests** are **dynamic** endocrine tests, which rely on the **physiological suppression** of **pituitary ACTH** and **serum cortisol** by

exogenous dexamethasone in **physiological** states, but **not in Cushing's syndrome**.

- The **dose** of dexamethasone required to suppress ACTH and cortisol will aid in determining the source of ACTH, and **differentiating ACTH-dependent** and **ACTH-independent Cushing's** syndrome.
- **Relative contraindications** to these tests include **diabetes** mellitus, **psychological disease**, and patients on **enzyme inducing agents such as anti-convulsants** who may **rapidly metabolize 'dexamethasone** and **decrease the sensitivity of the test**.
- Furthermore, **artificial oestrogens should be stopped prior to the test**, since they may induce cortisol-binding protein and artificially increase. Total cortisol levels.
- **Overnight dexamethasone suppression test** is an **alternative screening** tool for Cushing's syndrome, although it does **not reliably differentiate between Cushing's and pseudo-Cushing states**, or the source of ACTH.
- The test involves **administration** of **1 mg of dexamethasone** at **11pm**, and **measurement** of serum **cortisol at 8 am**

Distinguish Cushing's syndrome from pseudo-Cushing states

- **Low dose dexamethasone suppression test** has greater specificity than the overnight test, and hence distinguishes Cushing's and pseudo-Cushing states, but is more **cumbersome** than the overnight test.
- An **abnormal test**, **suggesting Cushing's syndrome**, involves the **failure to suppress** serum cortisol after **0.5 mg** dexamethasone administered **every 6 hours** for **48 hours.**

Determine the cause of Cushing's syndrome

- In a patient with confirmed Cushing's syndrome, an **undetectable serum ACTH** with a simultaneously **elevated serum cortisol** is **diagnostic of ACTH-independent Cushing's syndrome**.
- **If this combination s found** then other tests such as CRH test and **high dose dexamethasone** suppression tests are not necessary, and one needs to **proceed to imaging** the **adrenal glands.**
- **CRH test** can be performed **immediately after the low dose dexamethasone suppression test**, to **distinguish pituitary and ectopic ACTH production**.

- The basis of the test is the principle that pituitary tumours are responsive to exogenous corticotrophin releasing hormone (CRH), whereas adrenal and ectopic tumours are not.
- In pituitary Cushing's disease, the suppressed serum ACTH and cortisol at the end of low dose dexamethasone suppression should rise following CRH administration (conventionally by more than 20% of baseline).
- However, in adrenal Cushing's, the low ACTH and high cortisol levels at baseline are not affected by CRH.
- Similarly, in ectopic Cushing's, the high ACTH and high cortisol levels at baseline are not affected by ACTH.
- High dose dexamethasone suppression test is an alternative method of differentiating pituitary Cushing's disease from ectopic Cushing's syndrome.
- The test involves measuring serum cortisol after 2 mg of dexamethasone every 6 hours for 48 hours.
- Suppression of serum cortisol (conventionally by more than 50% of baseline) occurs in 75% of patients with Cushing's disease, although suppression also occurs in 10-25% of ectopic ACTH-secreting tumours, limiting sensitivity.
- Inferior petrosal Sinus Sampling is carried out in patients with Cushing's syndrome and elevated ACTH, in whom there is no clear pituitary source.
- The test involves sampling blood peripherally and from each inferior petrosal sinus under X-ray guidance and measuring ACTH in response to CRH administration.
- The aim of the test is to differentiate a pituitary and non-pituitary source of ACTH, and **lateralize** a corticotroph **adenoma**.
- If the Petrosal sinus ACTH is greater than peripheral ACTH, this indicates a pituitary source of ACTH.
- Additionally, if the ACTH level is greater in one petrosal sinus than the contralateral side, this localizes the pituitary tumour to the ipsilateral side.

Assess for complications

- **Glucose intolerance**: fasting glucose and oral glucose tolerance test
- **Osteoporosis**: bone density measurements

Tell me about Nelson's syndrome

- Nelson's syndrome was first described by Nelson and colleagues in 1958, and represents the **enlargement** of a **pituitary corticotroph adenoma** due to the **absence** of

negative feedback by adrenal cortisol production, following **bilateral adrenalectomy**.

- The defining clinical features are an **enlarging pituitary tumour** in the presence of an **elevated serum ACTH** and **hyperpigmentation**.
- The **pituitary corticotroph** cells also **produce** melanocyte stimulating hormone (**MSH**) which is responsible for the **hyperpigmentation**.
- Patients may also develop **bitemporal hemianopia** due to the rapidly enlarging pituitary tumour

Why is biochemical evaluation of Cushing's syndrome performed before imaging of the pituitary or adrenal glands?

- **Most cases of Cushing's disease** are due to **pituitary micradenomas** (<1 cm), and hence may not be clearly visible on MRI (**59% are seen on MRI**).
- Furthermore, the **incidence of incidental**, **non-functioning adrenal or pituitary adenomas is 10%,** which may mislead subsequent investigation and treatment.

What is the relevance of elevated serum calcium in a patient with a pituitary -adenoma?

- This may represent multiple endocrine neoplasia type 1 (MEN1).
- This is an autosomal dominant disorder characterized by **hyperparathyroidism**, **pituitary adenomas**, and **pancreatic islet cell tumours**.
- **Almost all** patients develop **hyperparathyroidism**, although pituitary and pancreatic lesions only affect 60%.
- The most common pancreatic lesion is a **gastrinoma** which may cause the Zollinger EIlison syndrome.
- The **MEN1 gene** has been identified and the gene product **'menin'**.
- However, unlike MEN2, **routine genetic screening** of family members is **not currently practiced** since there is little evidence that early diagnosis improves morbidity or mortality in the absence of symptoms.

Approach to the patient with suspected Cushing's syndrome:

- **Low clinical suspicion of Cushing's syndrome:**
    - Screening tests: Urinary free cortisol x3, or midnight serum cortisol, or overnight dexamethasone suppression test
- **High clinical suspicion of Cushing's syndrome:**
    - Low dose dexamethasone suppression test

- **If low ACTH and high cortisol:**
    - Adrenal imaging
- **To differentiate ectopic and pituitary ACTH:**
    - High dose dexamethasone suppression test, CRH test and MRI pituitary, or inferior petrosal sinus sampling

Clinical notes

- Avoid terms such as 'moon face' and 'buffalo hump'-these are not likely to endear you to the patient
- **Cushingoid facies** are due to **fat deposition in the cheeks**.
- When examining the patient from the front, one should look to see if the **cheeks obscure the ears** since this is part of the classical description of the cushingoid appearance
- **Fat deposition in the temporal fossae** also contributes to a rounded facial appearance
- **Fat deposition** in the **dorsocervical and Supraclavicular fat pads** is common and usually consistent with the degree of centripetal obesity.
- Supraclavicular fat pads make the **neck appear shortened** and **thickened**
- The **dermatological manifestations** of Cushing's syndrome include:
- **Skin atrophy**: **thinning of the stratum corneum**
- **Poor wound healing: secondary to skin atrophy**
- **Purpura**: **easy bruising** due to **loss of subcutaneous connective tissue**
- **Violaceous striae**: consequence of **skin stretching** due to **weight gain** and **impaired collagen synthesis**
- **Fungal infections**: **skin folds and nails**
- **Acne**: due to **increased androgens**
- **Hirsutism**: **increased hair in androgen-dependent regions** of the body (presenting feature in females
- **Hyperpigmentation** if very prominent, consider **Nelson's** syndrome or **ectopic** adrenocorticotrophic hormone (**ACTH**) production
- **Acanthosis nigricans**: velvety and hyper-pigmented skin in axillae, neck, and groin
- **Telangiectasia**: this may be seen as a **complication** of **topical steroid** use

- **Proximal myopathy** is almost universal in Cushing's syndrome, but is not typically present is pseudo-Cushing states, and is therefore a good **discriminatory sign**.
- Muscle weakness occurs due to the **catabolic effect of excess glucocortioids** on skeletal muscle.
- Initially ask the patient to **maintain their arms in an abducted** position, and **'don't let me move them'**.
- If there is no discernible muscle weakness in the upper limbs, ask the patient to **rise from a seated position without assistance**, looking for proximal muscle weakness in the **lower limbs.**
- **Bilateral adrenalectomy** is a largely historical treatment for **Cushing's disease** following the advent of **transphenoidal** pituitary surgery.
- While **bilateral adrenalectomy** is a **definitive cure** for **hypercortisolism**, the adverse consequences of adrenal surgery are lifelong mineralocorticoid and glucocorticoid replacement and the risk of Nelson's syndrome
- Since the retroperitoneal approach is the most common, look for scars on the back.
- If bilateral adrenalectomy scars are present look for skin pigmentation and ask to examine the visual fields (looking for bitemporal hemianopia).
- **Glucose intolerance** occurs due to **gluconeogenesis** from **glucocorticoid excess**, and **insulin resistance from obesity**.
- **Hypertension** occurs in all causes of Cushing's syndrome, but **is most marked in ectopic ACTH syndromes** where the **high serum cortisol concentrations** result in both **mineralocorticoid and glucocorticoid effects**
- **Marked pigmentation** is typically seen in patients with **ectopic ACTH syndromes**.
- The **mineralocorticoid effects** also cause **hypokalemia** which may exacerbate proximal muscle weakness.
- Tell the examiner you would like to look for **complications**, evidence of steroid-responsive conditions and ectopic ACTH secreting tumors:

Complications:

- **Diabetes**: finger pricks for glucose testing, diabetic retinopathy, glycosuria
- Hypertension: measure blood pressure, hypertensive retinopathy

- **Osteoporosis**: vertebral collapse (Kyphosis)
- **Cataracts**: secondary to **exogenous steroids** (not usually seen in endogenous steroid excess, except in children)

Steroid-responsive conditions:

- Asthma/COPD: wheeze, hyper-inflated chest
- Interstitial lung disease: clubbing, bibasal lung crepitations
- Rheumatoid arthritis: symmetrical arthropathy of small joints of the hands
- SLE: butterfly rash, arthropathy
- **Ectopic ACTH secreting tumours:**
    - **Small cell carcinoma of lung**: clubbing, nicotine staining, respiratory signs
    - **Carcinoid tumour**
    - Carcinoma of the pancreas

MRCP-PACES

Brief Clinical Consultation

Common Variant Immunodeficiency

You are SHO in GIM clinic
Mr. Edwardo is 25 years old with chronic recurrent cough

Confirmations:

- Self
- Patient
- Agenda

Opening question:

- You got troubled with cough
- Could you tell me more about it?
    - Yes doctor, I am suffering from this cough since last 2 years

Empathy and sympathy:

Brief analysis of cough:

ODPARA - OCD

- Any phlegm
- Color, amount
- Any coughing up of blood
- Any noisy chest
- High body temperature
- Excessive sweating
- Contact with sick patient
- Chest pain
- Any time during the day you cough more?
- **Association:**
    - Ringing ears
    - Need to clear you throat
    - Skin itchiness

    - Joint pain
    - Nasal coruscations

- Nasal bleeding
- Change in water work
- Loss of hair
- Pumps or lumps
- Weight loss
- Abdominal pain
- Any loose stool
- Difficult to flush

Drug history:

- Medication list
- Allergies
- Any vaccinations

Family history

- Chronic illnesses
- Similar conditions

Past medical history:

- Hospitalization
- I am receiving through needle some proteins every now and then to boost my body defense system

Surgical history:

- Social
- What is your job?
- QOL
- Any pets at home
- Any travel
- Do you have a partner?
- Smoking
- Sick leave

Can I examine you?

- **Chest:**
  - Coarse crackles all over
  - Not cleared on coughing
- **CVS** - P2
- **Abdomen**- splenomegaly
- **LNS**

- **Observation chart** - temperature
- ? Alopecia
- ? Skin ulcerations

What are your concerns?

- **Is it cancer?**
- **Is it going to kill me?**
- **What about my future children?**
- **I am working as tourist guide, why did I lose my hair?**
- **How this illness will impact my future?**
- From what you told me and after I examined you, most likely you have a condition called CVID in which your body lacks the enough defensive antibodies making you liable to get repeated bug infections in different organs and parts of your body
- These antibodies are belonging to proteins called immunoglobulins which are lacking in your body
- This means those affected cannot fight infection
- The outlook for patients with a CVID depends on how much damage has occurred to their lungs or other organs
- **This is not cancer**, but patient with CVID are prone also to get some types of cancer like the lymph glands cancer
- They are also likely to get problems like joint diseases and others like loss of hair.
- **The cause is not known**, and it can run in family that means your future kids can be affected
- We need to do some blood tests and images and to refer you to group of specialists including chest doctor, infectious disease doctor, physiotherapist, occupational therapist
- Regarding your future, you need to be very meticulous in dealing with any symptoms of infection and to go early to hospital to get appropriate treatment and to be keen with your follow up so not to get complications
- **Is that okay with you?**

What is your diagnosis?

- **Common Variant Immunodeficiency**

What are your differential diagnoses?

- 1- A gammaglobinemia
- 2- Hypogammaglobulinemia
- 3- HIV
- 4- Cystic fibrosis

How you will investigate this case?

- **Basic investigations**
  - CBC - platelets, Hb - autoimmune hemolysis or TCP
  - **Inflammatory markers**
  - **Sputum** - culture, G stain, AFB
- **To confirm diagnosis:**
  - **Serum IgA and IgG levels -**
    - Decreased - not absent
  - **Serum IgM levels**
    - Decreased occasionally
  - **T-cell function -**
    - Using anergy panel to assess localized immunologic skin responses
  - **Circulating T and B lymphocytes** can be assessed by using monoclonal antibodies for immunofluorescence staining.
  - CD19 and CD20 (B cells), CD3 (T cells), CD4 (helper T cells), and CD8 (suppressor T cells) are all commonly used
  - **T-cell activity** can be directly studied.
  - **Measuring the levels of mediators** and **cytokines** such as IL-2, IL-4, IL-5, **interleukin** 6 (IL-6), **interferon** gamma, and **tumor necrosis factor**
- **Radiology:**
  - CXR
  - HRCT of the chest
- **Pulmonary function testing**
- **LN Biopsy**
  - To exclude infection or malignancy in enlarging LNs
  - Histology:
    - Reactive follicular hyperplasia
    - Atypical hyperplasia
    - Granulomas
- **Bronchoscopy**

- **Endoscopy**

How are you going to manage this case?

Nonpharmacological:

- **Patient Education:**
  - Patients and their families should be educated about the early signs of infection so that aggressive treatment is not delayed

Pharmacological:

- **Immunoglobulin replacement**
- IV or S.C.
- **Solutions of 3-12% IV immunoglobulin** (IVIG)
  - Can be used on a regular basis to maintain a trough level of 400-500 mg/dL in adults.
  - A dose of 400-600 mg/kg every 2-4 weeks is usually required.
  - In patients with structural lung damage, a trough level of 700-800 mg/dL is required.
- **Antibiotics**
  - Dependent on sensitivity upon infection exacerbations
  - **Avoid prophylactic antibiotics**
    - Resistance
    - Predispose to fungal infection
- **Surgery:**
  - Chronic sinusitis
  - Splenectomy:
- Severe autoimmune TCO or hemolytic anemia

What are the complications of CVID?

- Recurrent infections
- Autoimmune phenomena
- Malignancy

What is the cause of death in CVID?

- A common cause of death in patients with CVID is **lymphoma**.
- **Other causes include**
- **Cor pulmonale** secondary to chronic lung infection
- **Liver failure** caused by viral or autoimmune hepatitis

- **Malnutrition** resulting from GI tract disease, and other viral infections.

MRCP-PACES

Brief Clinical Consultation

Dermatomyositis

Your role: **on-call in the MAU**
You are asked to see 30-year-old Mr. Edwardo who has presented with a **frequent fall**
Your task: to assess the patient's problems and address any questions or concerns raised by him.

Opening question:

- I got a letter from your GP mentioning that you have been troubled with frequent falls, could you tell me more about that
    - Yes, doctor I got great trouble recently, my legs are giving up
    - I cannot stand easily and unable to help myself any more

Brief analysis of fall:

ODPARA-OCD

May I know what do you mean exactly by fall?

- I am suffering from standing from sitting and very tough while trying to go back from the washroom
- I have noticed difficulty getting out of chairs and my family is concerned several recent falls.

Empathy and sympathy:

May I ask you few questions that may help in our discussion

- When did it start exactly?
- Was it sudden or gradual?
- Is it worsening or same since it started?
- Any weakness anywhere in your body?
- Any loss or altered sensation anywhere in your body?
- Any headache?
- **Any dizziness?**
- **Any loss of consciousness?**

- Any trauma to back?
- Any difficulty combing your hair?
- What about control of your water work and back-passages?
- Any **high body temperature**?
- **Any weight loss?**
    - Yes, I lost some weight recently
    - How much and over how long
    - Was it intentional?
    - What about your appetite?
- **Any joint pain?**
- **Any skin rash?**
    - Yes, I got rash on my face?
    - Is it itchy?
    - Is it painful?
    - Ny ooze?
    - Anywhere else you got rash.
    - In my knuckles of hands and neck
    - Is it related to sun exposure?
    - Can I have A look?
    - When you have a look, you got the heliotrope rash

Screen for dermatomyositis:

From above down:

- **Dysphagia** - Any difficulty in swallowing?
- **Bulbar involvement –** change in voice, regurgitation of food to your nose from gullet
- **Muscle -** pains or aches
- **Respiratory symptoms -** Lung malignancy and interstitial lung disease → breathlessness, cough, noisy chest, phlegm, chest pain, coughing up blood
- **–** any cough or coughing up of blood?
- **Raynaud's Phenomenon –** any change in color of your hands when exposed to cold?
- **GIT- motility disorder** → loose motion, **GI malignancy**, blood in back passages, tummy pain

- Dermatomyositis can be associated with esophageal neoplasia and esophageal dysmotility including reflux symptoms.
- **Joints –** arthralgia

Drug history

- **What treatments has the patient tried**
  - Topical, oral - including steroids, antibiotics, avoiding precipitants, and how did the patient get on with them?
  - **Did they help, and how?**
- Ask about use of **herbal and alternative remedies**
- Ask about **OCP use in younger women**
- Ask about **allergies**

Past medical history

- **Any previous episodes of skin complaints**
- Any evidence of **atopic conditions**, e.g. hay fever, asthma, eczema/dermatitis
- **How does patient's skin react to sunlight/use of sunblock**?

Family history:

Social history:

- What he does for living?
- With whom he lives?
- Support needed – climbing stairs m grills in toilet
- How is home condition?
- Alcohol
- Smoking

Can I examine you?

Start by patient concern

- **Proximal myopathy**
  - Ask the patient to stand from the chair without using his arms
  - Ask them to raise their arms above their head
  - There is **muscle tenderness**
- **Skin rash**
  - Adequately exposed the patient to see the rash
  - **Hands**:

- **Gottron's papules**
  - Erythematous, violaceous raised papules and plaques over bony prominences, e.g. extensor surfaces of phalanges, elbows, feet, and knees).
- **Nailfold erythema** due to **enlarged capillaries**
- **Periungual telangiectasia**.
- **'Mechanic's hands'** – roughened cracked skin on palms/sides of hands

- **Face:**
  - **lilac 'heliotrope' rash** on face **around eyelids**, **cheeks,** and other **sun-exposed regions** (including metacarpophalangeal [**MCP**] joints and **trunk**)
- **Body:**
  - **Telangiectasia**
  - **hyperpigmentation** in sun exposed areas (the **V-sign rash is discrete** and confluent macular erythema in a V shape in the **sun-exposed areas of the chest and neck**
  - **the shawl sign** is confluent **macular erythema** in the distribution of a shawl (the upper back, posterior neck, and shoulders)

- **Chest:**
  - Lung fibrosis/interstitial lung disease
- **CVS:**
  - **Myocarditis**
- **Hands:**
  - **Raynaud's phenomenon**
  - **Calcinosis**
  - Arthralgia
  - **periungual telangiectasis** - dilated nail-fold capillaries
  - Hyperkeratosis of the palms - **mechanic's hands**
- **Poikiloderma**
  - **hyperpigmentation** and **telangiectasias** on sun-exposed skin.
- **Buccal –** white plaques
- **Scalp** involvement with non-scarring **alopecia**

- **Ichthyosis**
- **Calcinosis** = unusual in adults, commoner in children and adolescents
- **Check temperature** (fever can occur in 20%)

- **I would like to examine the patient completely**, including a full **neurological** exam
- And examine abdomen and LNs looking for neoplasia

What are your concerns?

What is wrong with me?

- From what you told me and after I examined you, most likely you have a condition called dermatomyositis
- It is a condition affecting your muscles as well as the skin leading to your weakness and the falls
- The exact cause is not known but likely due to defect in your body defense system
- We need to investigate why you have developed this, and I would recommend we carry out some blood tests and imaging
- We will refer you to group of specialists to give you the best plan of management including joint doctor, skin doctor, chest doctor, bowel doctor for your difficult swallowing and physiotherapist together with occupational therapist who will assess your home condition And also will refer you to speech and language therapist – in case of bulbar involvement
- Will give you appointment to discuss you results of above tests
- Is that okay with you?
- Do you have any other concern?

Why is the food getting stuck?

- Swallowing problems are due to a range of causes, and we need to arrange some tests to find out what is causing your difficulties.
- This rash can be associated with problems with the muscles in the gullet pumping food down.
- We need to arrange an endoscopy test to look down the gullet and rule out narrowing, etc.

What can I do to get back on my feet?

- We need to find the cause for the weakness and treat it but will probably also **need to give you some steroid** tablets to **reduce the inflammation** in the muscles which is making you weak.

Questions commonly asked by examiners?

What are your findings?

- This gentleman has a characteristic **rash** of dermatomyositis in form of:
    - **Heliotropic rash:** a violaceous discoloration over the eyelids and face
    - **'Shawl' rash**: an erythematous eruption over the anterior chest and upper torso.
    - **Gottron's papules**.
        - There is often a **slight scale over them**
        - In some cases, a thick psoriasiform scale may be present.
        - They are found **over bony prominences**, **particularly** the **MCP**, proximal, and **DIP** joints, **elbows**, **knees**, and feet
    - **Nailfold telangiectasia**
- **Subcutaneous oedema** - mainly around the eyes and due to a transient increase in capillary permeability
- **Muscle features:**
    - **Proximal muscle weakness**
    - **Tenderness** of muscles
    - Muscle **wasting absent or minimal**
    - **Weakness of neck flexors** - two-thirds of cases
    - **Intact or absent deep tendon reflexes**

What is your diagnosis?

- The diagnosis is **dermatomyositis**.

What are your differential diagnoses?

- **The differential diagnosis of a periorbital rash includes:**
    1. **seborrheic dermatitis**
    2. periorbital **contact allergic dermatitis**
    3. Ocular **rosacea**.
- **The differential diagnosis of proximal muscle weakness with or without elevated muscle enzymes**
    1. **Amyotrophic lateral sclerosis** (MND)
    2. **Myasthenia gravis**
    3. **Muscular dystrophies**

1. **Inclusion body myopathy**, **vasculitis, overlap syndromes** (lupus, RA, scleroderma)
2. **Endocrine** – hypothyroidism, Cushing's
3. **Electrolytes** – low K, Mg, Ca, Na
4. **Infections** – viral (including **HIV**), fungal, bacterial or parasites
5. **Rhabdomyolysis**
6. **Drug-induced myopathy**
7. Polymyalgia rheumatica
8. Muscular dystrophy
9. Osteomalacia

- **The differential diagnosis of skin rash**
    10. Eczema
    11. Psoriasis
    12. SLE
    13. Rosacea
    14. Drugs and toxins
    15. Paraneoplasia

How would you investigate this patient?

- **Basic investigations:**
    - **Blood tests**
        - CBC
        - CK, ALT:
            - CK elevated (muscle enzymes) unless muscle not affected/involved
            - Estimation of serum creatine kinase (also known as creatine phosphokinase) levels (mirrors disease activity)
        - Inflammatory markers – ESR, CRP
- **Autoimmune screening:**
    - **Anti-Jo1 antibodies**
        - **Positive in 80%**
        - Highly **specific**
        - Antisynthase syndrome, fever, arthritis, myositis, fever, Raynaud's ILD
    - **ANA** is positive in **40%** of patients but has a **low specificity**.
    - **Anti-Mi2** (chromosomal helicase DNA binding protein)
    - **Anti RNP, Anti Ro**

- **Investigations for muscle disease:**
  - **EMG**
    - **Electromyography** shows **myopathic changes**
      1. Spontaneous fibrillation
      2. Salvos of repetitive potentials
      3. Short duration of polyphasic potentials of low amplitude
  - **MRI and MR spectroscopy**
    - of affected tissue may show **abnormal signals** in striated muscle and **abnormalities of muscle metabolism**.
  - **Muscle biopsy**
    - Gold standard for diagnosis
    - Show **necrosis**, phagocytosis of muscle fibers, and interstitial and perivascular infiltration of **inflammatory cells**
- **12-lead electrocardiogram**
  - May demonstrate **myocarditis** or **AV block** in the appropriate clinical setting.
- **Skin biopsy**
  - Skin biopsy: not diagnostic but may be supportive
- Importantly, a diagnosis of dermatomyositis would prompt an appropriate search for **underlying malignancy**.
- **Upper GI endoscopy** – for dysphagia
- **Lower GI endoscopy** – for motility disorder
  - Need to urgently investigate causes of weight loss and dysphagia, initially with upper GI endoscopy; important to investigate for associated malignancy
  - If esophagogastroduodenoscopy (OGD) normal, **barium swallow** may demonstrate **esophageal dysmotility**
- **HRCT**
- Other investigations may also be required, particularly given the significant smoking history (**CXR +/− CT chest**)

What is the treatment for dermatomyositis?

General measures

- Patient **education**
- **Bed rest** for patients with severe muscle inflammation
- **Physiotherapy** for muscle weakness - prevents contractures

Muscle disease

- **Bedrest** if severe muscle inflammation
- **Physiotherapy**
- May present with **pseudohaematuria** due to **myoglobulinaemia**
- **High dose steroid therapy**
    - Most patients respond to steroids
    - Prednisolone is the first-line drug for the empirical treatment of polymyositis and dermatomyositis
    - **Need bone protection**
- **Steroid sparing:**
    1. Methotrexate
    2. Azathioprine
    3. mycophenolate mofetil
- **High dose intravenous immunoglobulins**
    - Often for **6 months**
    - For **refractory cases**

Skin disease

- **Avoid sunlight** and use **sunscreen**
- **Oral steroids**
- **Hydroxychloroquine**
- Methotrexate or mycophenolate mofetil

Management of underlying malignancy

What is the prognosis?

- **Usually has a good prognosis** unless patient having advanced malignancy

What is dermatomyositis?

- This is an **idiopathic inflammatory myopathy** with characteristic cutaneous features.
- It frequently affects the joints, **esophagus (dysphagia**), and **lungs** (**interstitial lung disease**).
- Patients often present with skin disease.
- Muscle involvement may occur concurrently, precede the skin disease, or follow the skin disease by weeks to years_
- **Malignancy** is possible in any patient with dermatomyositis and should be sought for in **adults aged >40 years.**

What is dermatomyositis-sine myositis?

- Patients have **cutaneous manifestations without clinical evidence** of **muscle weakness** (normal serum muscle enzyme levels for at least 2 years)-

What drugs con induce dermatomyositis-like skin changes?

a. Hydroxyurea
b. Penicillamine
c. Statin
d. Quinidine
e. Phenylbutazone

What other skins lesions may resemble the appearance of Gottron's papules?

1. SLE
2. Psoriasis
3. Lichen planus

What would muscle enzymes demonstrate in a typical patient with dermatomyositis?

- Muscle enzyme levels are often abnormal except in patients with no muscle involvement.
- The most sensitive/specific enzyme is creatine kinase.
- Sometimes, elevation of the muscle enzymes precedes clinical evidence of myositis.

What is dermatomyositis/describe the pathogenesis?

- Dermatomyositis is an **idiopathic inflammatory myopathy** with **characteristic skin signs**.
- It is a **systemic disorder** that most frequently **affects the skin and muscles** but **may also affect the joints, the lungs** (interstitial lung disease), the **esophagus** (dysphagia), and **less frequently the heart** (myocarditis).
- Dermatomyositis can be associated with malignancy and this needs to be considered in the over 40 s.
- **Pathogenesis**: precise mechanisms for the pathogenesis of dermatomyositis are currently **unknown**.

What investigations would you carry out to investigate the dysphagia and weight loss?

- **OGD** followed by **contrast swallow** (**exclude neoplasia** first/**mechanical obstruction**, then look for **dysmotility**).

What are the side-effects of steroid therapy and how would you reduce the risk?

- Risk of steroid side-effects is **dose-dependent** and related to **duration** of therapy.
- Need, therefore, to prescribe the lowest effective dose for the minimum required period to minimize the overall dose.
- Consider the risk factors for some of the more **common side-effects** (e.g. **osteoporosis**, **diabetes, hypertension**), the effect of other side-effects on **lifestyle** / **quality of life** (e.g. **weight gain, cataracts**) and don't forget the **central side-effects** of insomnia, restlessness, altered mood and increased appetite.

Bone health:

- **lifestyle measures** to optimize bone health include an active lifestyle / weight bearing exercise, not **smoking,** or taking **excessive alcohol**, ensuring **adequate calcium intake in the diet +/− calcium / vitamin D supplementation**
- NHS Clinical Knowledge summary advises to **offer bisphosphonates** to **prevent osteoporosis** in
  - People who have been taking **oral corticosteroids for more than 3 months**, or
  - Who are likely to do so, and who are: **65 years of age or more**
  - **Less than 65 years of age with a previous fragility fracture**
  - Or **less than 65 years** of age without a previous fragility fracture and have a **T-score** of **−1.5 or less.**

- Need to **organize** a dual energy X-ray absorptiometry (**DEXA**) scan for **people less than 65 years of age** with **no previous fragility fracture** who have been **taking oral corticosteroids for 3 months or more**, or who are **due to start a course that is likely to last for 3 months or more**.
- Consider **starting treatment** if there is a **long wait for DEXA** scanning.
- If drug treatment is not indicated because the **T-score is between 0 and −1.5, repeat the DEXA scan in 1 to 3 years if corticosteroid use continues.**

Diabetes:

- If patient is known to have diabetes, then follow management plan closely including **monitoring blood glucose levels**.
- Drug therapy (insulin and/ or oral hypoglycemic drugs may need to be increased, or insulin started).
- If patient is **not known to have diabetes**, advise to **check for new onset of diabetes 1 month after initiation of oral corticosteroids**, **then every 3 months thereafter**.
- If possible, **dipstick test urine for glucose at each clinic visit**.

Other risks include:

- An **increased risk of infection** particularly on higher dose steroids
- **cataract**
- **glaucoma** development
- **peptic ulceration**, particularly in patients on aspirin or NSAIDs – check for dyspepsia and reflux symptoms as patients **may need a PPI** co-prescribed
- **proximal muscle weakness**
- **thinning of the skin**
- **facial changes (moon face)**
- **striae**
- **Delayed wound healing**.
- **Rarer** side-effects also include **aseptic / avascular necrosis of the hip.**

If patient on **steroids for over three weeks**, **supply** a **steroid card** (includes information on **preparation**, **dose** and **duration**, and **contact details of prescriber**).

- Prescribe the **dose in the morning** to **reduce effects on sleeping**.
- With patients on **steroids for over three weeks** you need to consider the **risk of adrenal insufficiency**, so **withdrawal** has to be **gradual** and clearly prescribed and explained to patients.
- **Patients on long-term steroids**, or who have been **on steroids in the previous year,** need advice on how to **adjust their steroid dose if unwell/ infection, undergoing surgery, extensive dentistry**, etc.
- Addison's Disease Self Help Group's 'Owner's Manual' is a useful practical guide for patients regarding this – see the section on 'crisis management'. See also Section I, Station 5, Skin, Case 6.

In which other conditions is there proximal muscle weakness with high serum creatine kinase levels?

- It may be caused by **drugs** such as **lovastatin**, **chloroquine and colchicine,** especially in patients on chronic haemodialysis.
- Remember that **steroids cause proximal muscle weakness** with **normal serum creatine kinase levels**.

How would you classify polymyositis–dermatomyositis?

- The classification of Bohan et al. is into **five groups**:

1. **primary idiopathic polymyositis**
2. **primary idiopathic dermatomyositis**
3. **dermatomyositis** (**or polymyositis) associated with neoplasia**
4. **childhood dermatomyositis (or polymyositis**) **associated with vasculitis**
5. **polymyositis (or dermatomyositis) with associated collagen vascular disease**.

Mention a few disorders associated with myositis

- **Sarcoid** myositis
- **focal nodular** myositis
- **infectious** polymyositis (Lyme disease, toxoplasma)
- **inclusion body** myositis
- **eosinophilic** myositis

What do you know about inclusion body polymyositis?

- **Inclusion-body myositis** usually occurs in **men >50 years** of age.
- It is characterized by **indolent**, **progressive proximal muscle weakness**, which **may be asymmetric**, that **eventually** also **involves distal muscles**.
- Both **myopathic and neuropathic changes** can be seen on **electromyography studies**.
- Muscle biopsy reveals **mononuclear infiltrates** and **vacuoles** in the muscle cells that contain **inclusion bodies**.
- Inclusion body myositis **often responds poorly to conventional therapy** with **steroids**.

What do you understand by the term overlap syndrome?

- Overlap syndrome indicates that **characteristics of two different disorders** are common to both.
- **Dermatomyositis overlaps** with **systemic sclerosis** and **mixed connective tissue disease**.

- Specific **signs of systemic sclerosis** and **mixed connective tissue disease**, such as **sclerotic thickening of the dermis**, **contractures, esophageal hypomotility**, **microangiopathy** and **calcium deposits**, are **present in dermatomyositis**.
- Patients with the **overlap syndrome of dermatomyositis** and **systemic sclerosis** may have a **specific anti-nuclear autoantibody**, anti-**PM/Scl,** directed against a nucleolar protein complex.

Notes

- **Male to female ratio is 2:1.**
- **Association with malignancy** (the current recommendation is that patients **over 40 years** of age with **dermatomyositis** should be **investigated** for an associated **malignancy** particularly in the **breasts, ovary, lungs,** and **GI tract**)
- **Overlap with rheumatic fever**, **rheumatoid** arthritis, **scleroderma**, **lupus** erythematosus and other **connective tissue diseases** may occur (**steroid responsiveness more likely**)
- **Signs of other connective tissue diseases** more common than in pure polymyositis
- **Dysphagia** due to upper oesophageal involvement
- **Raynaud's** and **arthralgia** are frequent
- **Subcutaneous and intramuscular calcifications** may occur
- Helpful **investigations** include serum muscle enzymes (**CPK and aldolase**), **urinary creatine**, electromyography (**EMG**) (**fibrillation**, **polyphasic action potentials** and in some patients **high-frequency bizarre repetitive discharges**) and **muscle biopsy.**
- The erythrocyte sedimentation rate (**ESR**) is **often normal despite active disease**

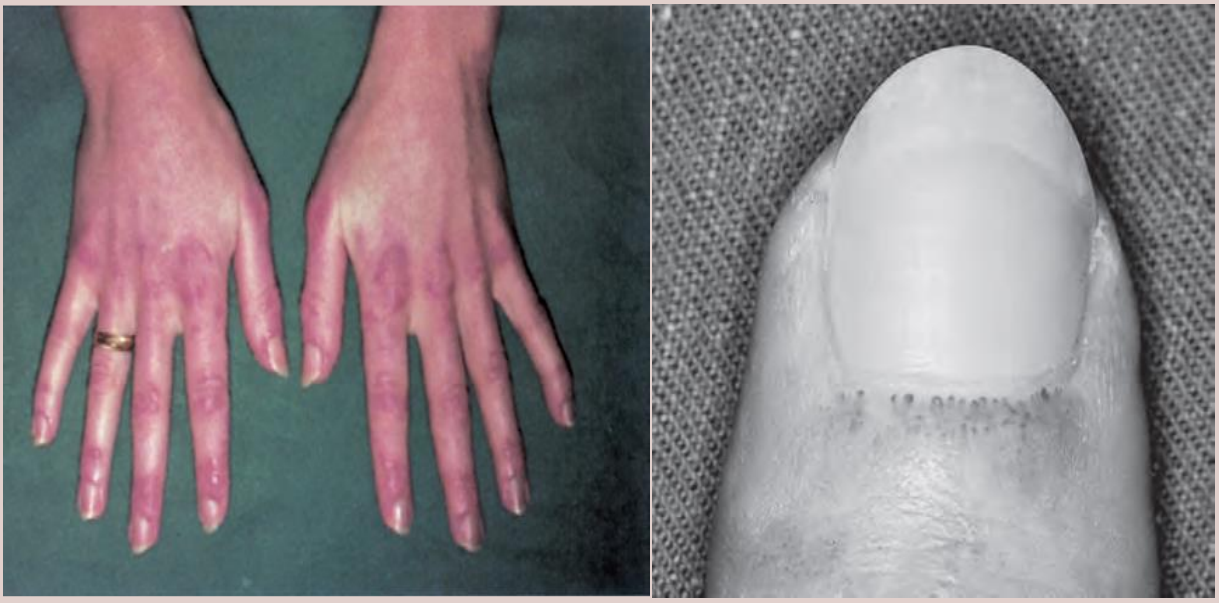
- In **patients >40** consider underlying **malignancy**.
- **Lung, breast, gastrointestinal tract**, and ovary are the **commonest** associations.

- Drugs- chloroquine, steroid, alcohol, statin, hydroxyurea
- The **adult form usually** occurs **after the age of 40 years**
- **Dysphagia** (caused by weakness of the muscles of the pharynx)
- **Dysphonia**
- **Muscle pain and tenderness**
    - **erythema of knuckles** accompanied by a **raised violaceous scaly eruption** (**Gottron's** sign); the erythema **spares** the **phalanges** (unlike that of **SLE** in which the **phalanges** are **involved** and the **knuckles** are **spared**)

- **Erythematous rash** may be present on the **neck** and **upper chest** (often in the **shape of a V**), **shoulders** (**shawl sign**), **elbows**, **knees** and **malleoli**
- **Cuticles may be irregular**, **thickened** and **distorted**; the **lateral** and **palmar areas** of the **fingers** become **rough** and **cracked** with irregular '**dirty'** horizontal lines, resembling those in a **mechanic's hands**.

- If the **patient is >40** years, tell the examiner that you would like to look for an **underlying neoplasm**.
- Look for **interstitial lung disease** (occurs in **5–10% of patients** with **polymyositis or dermatomyositis**, especially in those with **anti-Jo-1 antibody**).

Note the characteristic distribution of the rash.
Note the oedema and heliotrope discoloration around the eyes.



(c) **Gottron's papules: flat-topped**, **violaceous papules** over the **knuckles** and **interphalangeal joints.**
(d) **Nailfold telangiectasia** is characteristic.

Figure 5.33 Dermatomyositis. Photosensitive rash in a patient with dermatomyositis. Note the well demarcated **rash** in a **sun exposed area** of the chest.

Figure 5.34 Dermatomyositis.

- This patient's finger demonstrates **periungual erythema**

Figure 5.35 Heliotropic rash.

- There is a **peri-orbital violaceous hue** consistent with dermatomyositis.

Figure 5.36 Hand signs in dermatomyositis.

- **Gottron's papules** are present on the **dorsal aspect** of the **metacarpophalangeal and proximal interphalangeal joints**.
- There is also rough, dry skin on the fingertips and ragged cuticles, colloquially known as **mechanic's hands**.

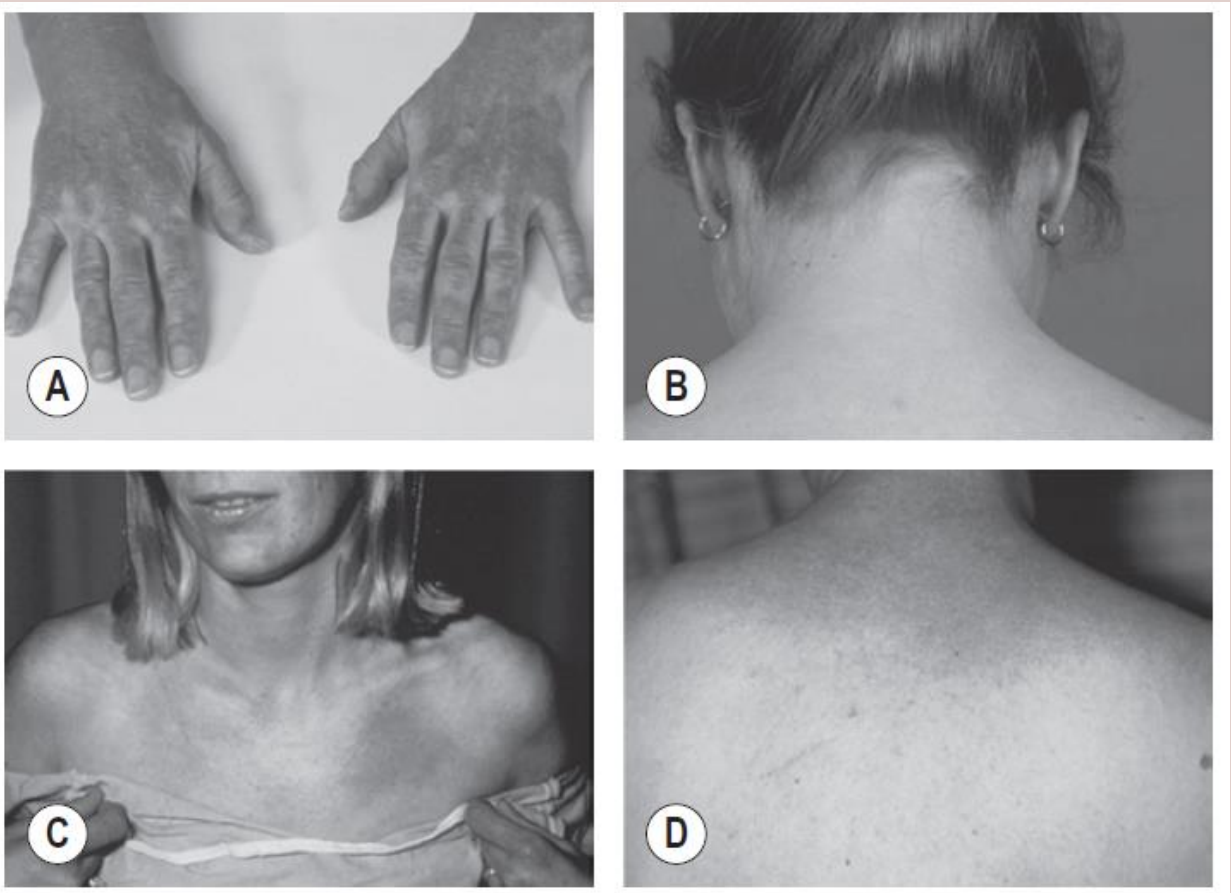


Fig. 63.1 Characteristic dermatomyositis skin changes. (A) Linear erythema (Gottron's sign). (B) Scalp rash. (C) V sign. (D) Shawl sign. (With permission from Firestein et al. 2008.)

Anecdotes

- **Classical dermatomyositis**.
- I had never seen this except in photographs and I almost missed it.
- She looked ‘autoimmune’ with white hair, pale skin and **purplish eyelids and knuckles**.
- I pointed this out but could not give a diagnosis.
- I was then asked to examine her arms where she had a small, healing, **surgical scar over the triceps**.
- Once I had ‘clicked’ that this was a **muscle biopsy** the diagnosis was easy. By now I was thoroughly enjoying myself and I turned to one of the examiners and said, ‘I almost missed that’. ‘Yes,’ he said, ‘but you didn’t!’

- I was then asked to look at a man’s hands.
- He had classic dermatomyositis and I described it as such.
- However, I had to be prompted to test for muscle power which was much reduced.

MRCP-PACES

Brief clinical consultation

Deterioration in renal function

You are an **ST2** covering the **medical wards on-call**.
You have been asked to see **Dina Salmon**, a **65-year-old woman** with DM and HTN who was admitted 3 days ago with a **UTI**, but the nurses are concerned about her **poor urine output.**
BP 100/75, pulse 96.
Today's blood tests have shown U&E 20, **creatinine160, eGFR 30.**
Your task: to assess the patient's problems and address any questions or concerns raised by her.

Confirmations:

- Self
- Patient
- Agenda

Opening question:

- **You got troubled with bug infection in water work could you elucidate more to me with that regard?**
    - Yes doctor, I got severe burning pain in my water work
    - And since I did not improve, I got admitted now, I do not know what that happening?

Empathy and sympathy:

Analysis of complaint:

- Any high body temperature?
- Any sweating?
- Are you passing more water than usual?
- Yes, I am going frequently now to toilet
- What the color of your water?
- Any blood in urine?

- Any passage of gravels?
- Any back pain or flank pain?
- Any syncope?
- Any antibiotics given?
    - Yes, I had not got better on cefalexin and the pain worsened so you came to hospital.
- Are you better now?
- Analysis of increased RFT results:
- Are you feeling sick or getting sick?
    - I have thrown up everything I took last night
- Any loose motion?
- What about fluid intake?
    - Getting less now, feeling sick
- Any fluid through needle?
    - No, it got stopped yesterday
- Any pain medicine now?
    - yes, naproxen 500mg bd
- Any test done?
    - water work showed a bug called E. coli
- **Was kidney test okay before?**
- Any skin rash - Strep GN?
- Any visit to kidney doctor?
- **Risk factors for renal disease:**
    - DM, HTN
- **Vascular disease** - ask about history of
        - Strokes/TIA
        - Heart attack
- **Any recent instrumentation of urinary tract** - risk of infection

Past Medical History:

- DM
- HTN
- **Any kidney problem?**
- ? Kidney stone last year
    - CT no stone

Drug history:

- Ramipril 5mg twice per day
- Metformin 1 g bd
- Occasional paracetamol for arthritis
- Any allergies
- Any NSAIDs

Social history:

- Live alone
- Daughters live nearby
- Independent
- Retired bank clerk
- Non-smoker
- No alcohol

Family History:

- Mother died from a stroke age 75
- No family history of diabetes
- Kidney disease

Can I examine you?

- GCS/LOC
- **Drowsiness** or confusion -Uraemia
- RR/pattern, e.g. **Kussmaul respiration** due to acidosis
- Temperature - apyrexial
- **Fluid balance** - hypovolemic
- **Assess circulation:**
    - Pulse - Pulse 80
    - Capillary refill
    - Peripheral perfusion
    - BP- low in shock - BP 110/70
- **Assess JVP at 45°**
- **Nailfold infarcts - vasculitis**
- Rash:
    - Petechial rash in streptococcal sepsis; vasculitis/Henoch–Schönlein purpura
- **Chest:**

    - Basal crackles: pulmonary edema
- **Abdomen:**
    - Tenderness - suprapubic/renal angle
    - Bladder palpable?
- Leg, sacral and scrotal edema
- Offer **urine dip stick**
- **Fluid balance chart**

Do you have any concerns?

What is wrong with me, doctor?

- You have been on treatment for an **infection in your water work,** which is more common in people with diabetes, but the blood results show that your kidneys are not working now as well as they were.
- This is likely to be **due to a combination of things** – the infection, losing fluid through getting sick, not eating, and drinking as much as normal, and the BP medications.
- We need to continue to treat the infection but also give you some fluids through the needle, anti-sickness injections and stop some of your medicines temporarily to allow your kidneys to recover back to normal.
- I will also request a scan to check that the kidneys are draining properly.
- Will also involve the kidney doctor
- **Is that okay with you?**

I am worried about my blood pressure.

- My mum had a stroke which the doctors put down to her blood pressure.

Don't I need these tablets?

- Now your BP is low.
- We will monitor your blood pressure and your blood results to see how the kidneys improve with treatment – we can restart BP medications if you need them once your kidneys have improved.

Will my kidneys recover?

Will I need dialysis?

- Kidneys often get affected by urine bug infection and fluid loss, and medicines also affect the kidneys.
- We are treating the bug infection with antibiotics, rehydrating you with fluids
  through the needle, and will give you medicines for feeling sick so that you can eat and drink.
- I expect your kidneys to improve over the next few days and we will keep you informed of progress.
- Rarely, people's kidneys do not improve as expected and need to be supported with dialysis.
- I think that your kidneys will improve with the treatment we are giving as they were working normally when you came into hospital, but we will need to keep a close eye on you

Examiners' questions:

What are your findings?

- The gentleman is euvolemic but negative fluid balance on chart

What is your diagnosis?

- AKI for differential diagnoses of the cause

What are your differential diagnoses?

1. **Acute kidney injury:**
   - Urinary sepsis / pyelonephritis (E. coli)
2. **Dehydration:**
   - Reduced intake
   - Increased losses- vomiting
3. **Drug induced:**
   - NSAIDs
   - ACEI
4. **Chronic renovascular disease:**
   - DM, HTN - although baseline results normal

How you will investigate this case?

- **Basic investigations:**
  - ESR, CRP
  - FBC, CK

- Urinalysis
- ABG - lactate
- CXR to exclude pneumonia - nidus
- **Renal screen:**
    - ANA, ANCA
    - Immunoglobulins
    - C3/4
    - Protein electrophoresis
- **Urine:**
    Urinalysis
    Bence Jones protein - MM
- **US- KUB:**
    - Exclude obstruction
    - Assess renal size

How you will manage this case?

- **Nonpharmacological:**
    - Referral to renal physician
    - Urinary **catheter**:
        - Monitor urine output
        - Exclude urinary retention
- **Stop offending drugs** - NSAID and ACEI
- **Rehydrate** IV with crystalloid
- Correct **antibiotics** for urinary sepsis
- **Adjust medicines** as per creatinine clearance
- **Antiemetics**

What is the management of obstructive uropathy?

- Depending on the location of the obstruction
    - Catheter
    - Nephrostomy
    - Ureteric stent
- There will be a **polyureic phase** following relief of the obstruction which can lead to marked hypovolaemia, and strict fluid balance is required.

What are the components of the Sepsis 6 bundle (Surviving Sepsis Campaign) and why are the severe sepsis bundles advocated?

- **Reducing mortality** due to severe sepsis requires an organized process that guarantees early recognition and consistent application of evidence-based practices.
- The Severe Sepsis Bundles are a **series of therapies** that, when implemented **together**, **achieve better outcomes** than when implemented individually.
- The resuscitation bundle is a combined **evidence-based goal** that must be completed within 6 hours for patients with **severe sepsis**, **septic shock and/or lactate > 4mmol/L** (36mg/dL).
- The goal is to perform all indicated tasks 100% of the time within the first 6 hours of identification of severe sepsis.
- **The tasks are:**
  - Measure **serum lactate**
  - Obtain **blood cultures** prior to antibiotic administration
  - Administer **broad-spectrum antibiotic within 3h of ED admission** and within **1h of non-ED admission**
  - In the event of **hypotension** and/or a **serum lactate > 4mmol/L:**
    - deliver an initial minimum of **20mL/kg of crystalloid** or an equivalent
    - apply **vasopressors** for hypotension **not responding** to initial fluid resuscitation to **maintain (MAP) > 65mmHg**
- **In the event of persistent hypotension despite fluid** resuscitation (**septic shock**) and/or **lactate > 4mmol/L**
  - achieve a (CVP) of ≥8mmHg
  - achieve a central venous oxygen saturation (ScvO2) ≥70% or mixed venous oxygen saturation (SvO) ≥65%.

MRCP-PACES

Brief Clinical Consultation

Deterioration in Renal Function

Role: On-Call medical registrar
Mrs. Sandy is 58 years old, has been admitted to the medical ward with cellulitis of the left leg.
She has been on intravenous antibiotics (flucloxacillin and benzylpenicillin) for four days and has responded well to therapy. Her previous history includes type 2 diabetes and hypertension. Her glycaemic control was initially managed with an insulin infusion, but this has been switched back to her usual diabetic medication, which consists of metformin and insulin.
Her renal function on admission was normal.
Today, her blood tests have been phoned through urgently to the ward with Na 132 mmol/L, K 6.8mmol/L, Ur 34.1, Cr 651.
The patient feels well in herself and has not voiced any complaints. The ward sister who took the urgent phone call, has asked for an urgent medical review.
Task: Assess the patient, establish cause of renal dysfunction and advise further investigation and treatment

Confirmations:

- Self
- Patient
- Agenda

Check:

- Expectations
- Knowledge
- How she feels

Opening question:

- **I came to know that you have abnormal kidney function blood tests, could you tell me about that?**
- I have been admitted to the ward with severe skin infection of the left leg
- I have been treated with through needle antimicrobials for four days with good improvement
- Following the ward round earlier way, the consultant was keen to switch to oral antimicrobials from tomorrow.

- I have repeat blood tests today which show that my kidney function has deteriorated.
- However I feel well in myself.
- I don't know what is wrong?

Analysis of deterioration of kidney function tests:

- Are you feeling or getting sick?
- Any high body temperature?
- Has there been a reduction in urine output?
    - I noticed that over the last two days, I have passed very little urine.
    - Today at 6 am, I passed very little urine and have not passed any since.
    - I admit that I haven't been drinking much fluid recently as I was feeling unwell with the skin infection
- Any frothy urine?
- Any burning water work?
- Water work frequency?
- Any flank pain or tummy pain?
- What is color of your water work?
- Any passage of gravels?
- Any loose motion?
- Any chest pain
- Any SOB
    - I feel a little more breathless than usual.
- There are generalized aches and pains and you feel lethargic
- **Rheumatologic diseases:**
    - Any joint pain
    - Any skin rash
- **Are there any symptoms of uremia?**
    - Restlessness?
    - Itchiness?
    - Tiredness?
    - Confusion? (Metabolic encephalopathy)
    - Chest pain? (uremic Pericarditis)
- **Enquire about symptoms of fluid overload:**
    - SOB?
    - SOB upon lying down on bed?
    - SOB awakening you from sleep catching for breath?
    - Leg swelling?
- **Enquire about symptoms suggesting hypovolaemia:**
    - Fluid intake?
    - Loose motion?
    - Thirst?
    - Dizziness upon standing from sitting position?
- **Enquire about any recent investigations with contrast** (contrast nephropathy)
    - Anybody scans done recently

Past medical history:

- Any history of kidney disease?

- **Are you diabetetic?**
    - Is it controlled?
    - What about your diet?
    - What about last 3 months blood sugar reading
    - Any eye sight problem
    - Any Weakness anywhere in your body?
    - Any sensory loss?
    - Any heart attack?
    - Are you following regularly your diabetes doctor?
    - Are you exercising regularly?
- What about your previous kidney tests?
- I have regular diabetic checks and I have been told I have my kidney function previously has been normal, but at my last check I was told there was a slight increase in protein in the urine
- **Are you HTN?**

Drug history:

- Aspirin
- Simvostatin
- Ramipril
- Frusemide
- Metformin
- Insulin.

Family history:

- Family history of kidney problems
- Last year, my mother was admitted with pneumonia and her kidney function deteriorated significantly.
- The doctors said she had renal failure.
- She had to be admitted to the intensive care unit for dialysis.
- I am becoming increasingly worried that I may also have renal failure.
- What is your job?
- Alcohol
- Smoking

Can I examine you?

- Review observation chart
- Heart rate, blood pressure, and oxygen saturations
- Fluid balance charts
- Urine output (if documented)
- Glucose readings (renal failure result in reduced insulin metabolism thus predisposes to hypoglycaemia)
- **Examine fluid status**
    - **Hypovolaemia**
        - Raised JVP
        - Third or fourth heart sound
        - Bibasal lung crepitations
        - Edema
    - **Hypovolaemia**
        - Reduced JVP
        - Dry mucous membranes
        - Reduced skin turgor

- **Examine for uremia**
    - Restlessness and confusion
    - Pruritis
    - Flapping tremor of outstretched hands (metabolic encephalopathy)
    - Pericardial rub (uremic Pericarditis)
- **Examine abdomen**
    - Palpable kidneys (polycystic kidney disease)
    - Palpable bladder (urinary retention)

What are your concerns?

(o) What is the cause of the deterioration in kidney function?
(b) Do I have renal failure?
(c) Will I need to have dialysis?

- From what you told me and after I examined you and checking your kidney function tests, you have a condition called kidney failure in which the kidneys are not working properly
- The most likely cause is lack of fluids
- We need to do some blood tests and imaging to confirm our diagnosis
- Will give you fluid through needle and will monitor your kidney function and will refer you to kidney doctor and to gland doctor also to follow-up you regularly for blood sugar
- As a result of poor- kidney function, a blood salt, called potassium level in the blood is high and this needs treatment.
- Although the most likely cause is dehydration, other causes of renal failure need to be excluded.
- Further tests will be necessary, including blood tests, heart tracing, urine tests, and kidney scan.
- It is important to initiate through needle fluids, and closely monitor the urine output carefully and this will require insertion of a urinary catheter.
- At this stage, it is difficult to tell whether dialysis will be needed, but this will largely be determined by the response to adequate rehydration.
- A repeat blood test will be requested following rehydration and correction of the potassium level

Questions commonly asked by examiners

What is your diagnosis?

- Acute renal failure (pre-renal)

What are your differential diagnoses?

- **Pre-renal:**
    - Hypovolaemia
- **Renal**:
    - Glomerulonephritis
    - Tubulointerstitial nephritis
    - Acute tubular necrosis
- **Post-renal:**
    - Urinary obstruction

- In this patient, the **most likely cause is pre-renal** due to **hypovolaemia** (**poor fluid intake** with concurrent **diuretic** therapy).
- Another possibility is **Tubulointerstitial nephritis** secondary to **penicillins**.

How you will investigate this case?

- ECG (to look for features of hyperkalaemia)
- CXR (if suspecting fluid overload with pulmonary congestion)
- Blood **tests**
    - Establish acid-base status
    - Repeat U&E after intravenous fluids and correction of hyperkalaemia
    - Autoimmune profile
    - ESR
    - Calcium and phosphate
    - **CK**
    - **Serum protein electrophoresis**
    - Serum bicarbonate
- **Urine tests**
    - Urinalysis
    - Urine microscopy for cells, crystals and casts
    - Urine for Bence-Jones protein
    - Urine osmolality
    - Urine: Plasma osmolality ratio
    - Urine: Plasma creatinine ratio
    - Urinary sodium
- **Ultrasound scan of the renal tract**

How you will manage this case?

- Stop nephrotoxic medications
- Adjust antibiotic doses for renal dysfunction*
    - If the cause of renal failure is penicillin therapy then one would consider stopping penicillin, and replacing with alternative antibiotics if clinically indicated.
- However, the most likely cause is pre-renal (dehydration) and given that strong clinical indication for antibiotic therapy (severe cellulitis), then it is appropriate to continue penicillin in the first instance but to make dose adjustments for renal dysfunction.
- Correct hyperkalaemia (calcium gluconate and insulin/dextrose infusion)
- Intravenous fluids to optimize volume status (this may require monitoring o f central venous pressure)
- Urinary catheter to monitor hourly urine output
- **Stop metformin**-Insulin infusion to optimize glycaemic control.
- Monitor glucose closely
    - Insulin is metabolized by the kidneys.
    - In acute renal failure, the insulin requirement therefore decreases.
    - This must be remembered when correcting hyperkalaemia with insulin/dextrose infusions and using insulin infusions for glycaemic control.

        - It is important to monitor glucose carefully in this setting, and beware of hypoglycaemia.
    - Accurate fluid-balance charts
    - If persistent oliguria or anuria, despite optimization of fluid status, then consider hemofiltration

What are the indications for haemofiltration in acute renal failure?

- **Refractory acidosis**
- **Refractory hyperkalaemia** (despite adequate treatment)
- **Pulmonary edema**
- **Uremic encephalopathy**

How can you differentiate between pre-renal renal failure and renal failure due to intrinsic (renal) disease?

- In renal failure due to intrinsic disease, the kidneys lose the ability to concentrate urine and sodium excretion is inappropriately increased.
- In pre -renal renal failure, the ability to concentrate urine is preserved

	Pre-renal	Renal
Urine osmolality	>500	<350
Urine: Plasma osmolality	> 1.5:1	< 1.1:1
Urine: Plasma creatinine	>20:1	< 20:1
Urinary sodium	<20mmol/L	>50mmoi/L

What do you know about the different types of urinary casts?

- Tubular casts: acute tubular necrosis o r interstitial nephritis
- Hyaline casts: Tamm-Horsfall glycoprotein
- Granular casts: non-specific
- Red cell casts: glomerulonephritis
- White cell casts: acute tubular necrosis or pyelonephritis

MRCP-PACES

Brief Clinical Consultation

Diarrhoea – C. difficile

Role: **On-call medical registrar**
55 years, Mr. Edwardo has been an inpatient on the respiratory ward for four days
He was admitted with **severe community acquired pneumonia** and has responded well to antibiotic therapy with amoxicillin and clarithromycin and supplemental oxygen therapy
He has **developed diarrhoea** over the last three days. Initially this was mild and settled but has returned today
He has had four severe episodes since this morning.
He complains of diffuse abdominal pains and cramps
The ward nurse has taken routine observations and noted a pulse rate of 98 beats per minute and a blood pressure of 98/50
She is concerned that he is dehydrated and has requested o medical review.
Task: Assess the patient and advise on further therapy.

Confirmations:

- Self
- Patient
- Agenda

Opening question:

- You got troubled with watery stool
- **Could you tell me more about it?**
  - I have been admitted to the respiratory word with bug infection in chest and have responded well to through needle antibiotic
  - I have been an inpatient for four days.
  - On the second day of admission I developed loose stool, but this settled.

- However, since this morning you have had four Large episodes of watery stool.

Empathy and sympathy:

Analysis of watery diarrhoea:

ODPARA

- Onset
- Frequency (day and night)
- Normal bowel habit
- **Consistency**
- Duration
- Progression
- **Association:**
  - Vomiting
  - Cramps, distension
  - **Abdominal pain**
    - There is generalized abdominal pain with severe cramps
- Blood - no
- Slime - no
- Feeling sick
- High temperature
- I feel thirsty
- **Any contact with patient who has diarrhoea**
- Unintentional weight loss
  - 1stone over the last year
  - Loss of appetite
- **Chest infection:**
  - **Risk factors for legionella:**
    - Inhalation of aerosolized mist from water sources e.g. whirlpools, showers, cooling towers, and air-conditioning systems

Past medical history:

- Similar condition

Endurance

- Constipation for two years
- I take regular senna and lactulose
- History of bowel disease - IBD
- Chronic respiratory disease - risk factor for Legionella
- Malignancy
- Hyperthyroidism

Family history:

- Bowel cancer
- In my father and uncle at age 72 and 74 years respectively
- My father died due to advanced cancer with metastases
- My uncle underwent curative surgery

Drug history:

- Any allergies
- Show me your medications
- Any **laxatives**?

Social history:

- Job
- Smoking:
  - Risk factor for Legionella
- Alcohol
- No history of **recent travel**

Can I examine you?

- **Review observation chart**
  - Heart rate
  - Blood pressure
  - Temperature - since admission
- **Fluid status:**
  - Mucous membranes
  - Skin turgor
  - JVP
  - Postural blood pressure
- **Asses nutritional status**

Endurance

    - Cachexia
    - Temporal wasting
    - Reduced triceps fold thickness
- **Examine the abdomen**
    - Abdominal distension
    - Abdominal tenderness
    - Examine for masses
    - Bowel sounds
- Clubbing (IBD and GI malignancy)

What is your concern?

Why I have this lose motion?

- From what you told me and after I examined you most likely your loose stool is related to antimicrobial you are getting for the chest bug infection, it's important to continue with the antimicrobial, since there has been a clinical improvement.
- The regular use of laxatives will be contributory, and this will have to be discontinued temporarily.
- The loose stool has resulted in loss of body fluid and giving fluid through needle is necessary.
- Oral antimicrobials are necessary to cover antibiotic-associated diarrhoea
- Further investigations will be necessary to exclude other possible causes like chest bug infection related loose stool
- We need to arrange blood tests, stool tests, and abdominal X-ray
- Is that okay with you?

What are your differential diagnoses?

1. **Antibiotic-associated diarrhoea**
2. **Diarrhoea secondary to atypical pneumonias:**
    - Legionella
    - Mycoplasma
3. **Bowel cancer**

Endurance

- Important feature in the history is altered bowel habit (constipation), weight loss of appetite, and a family history of bowel malignancy.

How to investigate this case?

- **Basic investigations:**
  - Urea and electrolytes
  - Inflammatory markers
- **Thyroid function tests**
  - Hyperthyroidism is a cause for diarrhoea.
  - This lady has had a long-standing history of constipation and it is important to exclude hypothyroidism as a potential cause.
- **Tests for atypical pneumonia:**
  - **Mycoplasma:**
    - Complement fixation tests
    - lgM antibodies
  - **Legionella:**
    - Urinary Legionella antigen
    - Direct immune florescence
    - PCR of respiratory specimens
- **Abdominal x-ray**
  - Ileus
  - Toxic megacolon
- **Stool tests**
  - Microscopy
  - Culture
  - C. difficile toxins

How are you going to manage this case?

- Intravenous fluids with **potassium** replacement if necessary
- Continue current **antibiotic** therapy - consider changing
- **Oral metronidazole** - first line
- **Oral vancomycin** - second line
- Withhold laxatives temporarily

- Recommend **outpatient investigations**, i.e. **colonoscopy** given a history of altered bowel habit, weight loss, and loss of appetite with a strong family history of bowel cancer

Questions commonly asked by examiners

What is the definition of antibiotic associated diarrhoea?

- This is defined as unexplained diarrhoea that occurs in association with antibiotic treatment.
- When does diarrhoea develop in antibiotic associated diarrhoea
  This can develop between 2 hours and up to 2 months after antibiotic use.

How common is antibiotic-associated diarrhoea?

- The incidence ranges between 5-25% depending on the type of antibiotic

What organisms are implicated in antibiotic-associated diarrhoea?

- Clostridium difficile (most common accounts for 25% of cases)
- Clostridium perfringens
- Staphylococcus aureus
- Klebsiella oxytoca
- Candida spp
- Salmonella spp

How can antibiotic-associated diarrhoea be prevented?

- Limit antibiotic use
- Probiotics:
  - Saccharomyces boulardii
  - Lactobacillus

endurance

How is C. difficile diagnosed?

- **Detection of stool cytotoxins A and B:**
  - ELISA based tests (false negative rate=10% - these tests increase negative predictive value
  - RT-PCR has high sensitivity and specificity for toxin B.
  - Stool culture is not commonly used, since 30% of hospitalized patients are colonized without disease, and anaerobic culture takes 3 days.

What is the management of diarrhoea associated with C. difficile?

- Stop causative antibiotic (this may not be possible if it is necessary to treat original infection; consider changing antibiotics to those less implicated in antibiotic associated diarrhoea:
  - Aminoglycosides
  - Sulfonamides
  - Macrolides
  - Vancomycin
  - Tetracycline
- Treat dehydration and correct electrolyte disturbance ·
- Avoid the use of anti-peristaltic drugs:
  - Loperamide
  - Opiates
- **Oral antibiotic therapy:**
  - ✓ **Metronidazole** (first line)
  - ✓ **Oral vancomycin** (second line)
  - ✓ **Fidaxomicin**, sold under the brand name Dificid among others, is the first member of a class of **narrow spectrum macrocyclic antibiotic** drugs called **tiacumicins**. It is a fermentation product obtained from an actinomycete. Fidaxomicin is **minimally absorbed** into the bloodstream when taken orally, is **bactericidal**, and selectively eradicates pathogenic Clostridium difficile with relatively little disruption to the multiple

species of bacteria that make up the normal, healthy intestinal flora. The maintenance of normal physiological conditions in the colon may reduce the probability of recurrence of Clostridium difficile infection

- Observe infection-control hospital guidelines

When should oral vancomycin be used?

1. Intolerant to metronidazole
2. Poor response to metronidazole
3. Pregnancy

Can metronidazole or vancomycin therapy be given - intravenously?

- Ideally the treatment should be oral since C. Difficile is restricted to the lumen of the colon.
- Only metronidazole (not vancomycin) can be given intravenously as this can result in adequate colonic concentrations

What are the complications of C. difficile infection?

- Pseudomembranous colitis
- Toxic Megacolon
- Ileus
- Perforation
- Shock

endurance

Endurance
18-11-2018

MRCP-PACES

Brief clinical consultation

Familial Mediterranean fever

Scenario:

You are SHO in clinic
Mr. Edwardo, 23 years old, complaining of **abdominal pain**

Confirmations:

- **Self**
- **Patient**
- **Agenda**

Opening question:

- You got troubled with tummy pain
- Could you tell me more about it?

Analysis of abdominal pain:

- **ODPARA-OCD:**
  - When did it got started?
  - Sudden or gradual
  - Where is the pain in your tummy exactly?
  - Does it go anywhere else?
  - How much you grade it from 0 to 10?
  - Anything makes it better?
  - Anything makes it worse?
  - What is the nature of this pain?
  - Aching, dull, burning, colicky?
- **Screen GI symptoms:**
  - Getting sick
  - Feeling sick
  - Loss of appetite
  - Acid brash
  - Difficulty in swallowing

- ❖ Hard or loose stool
- ❖ Yellow discoloration - gall stones

- **GUS:**
  - Passage of gravel in water work
  - Frothy water work
  - Burning urine
  - Red urine
  - Dark urine
- **Alarm symptoms:**
- **Malignancy:**
  - Weight loss
  - High body temperature
    - **Yes, I have high body temperature on and off**
  - Blood in back passages
  - Lumps and pumps
- **System review:**
  - ➢ Cough- TB
  - ➢ Altered sensation, weakness- porphyria
  - ➢ Chest pain: CAD, FMF
  - ➢ Joint pain: Felty, FMF

DH:

Surgical history:

- **Appendix removal**

FH:

- Similar condition

PMH:

- Any disease I should be aware of?
- Blood transfusions

Social history:

- Job
- QOL
- Alcohol
- Smoking
- Any support needed

endurance

Can I examine you?

- **Abdomen:**
    - Scars of surgery
    - Tender rigid abdomen
    - **Tender testis also ovaries**
- **Chest- pleural rub**
- **Observation chart - temperature**
- **Synovitis** - **arthritis**, warmth, erythema, swelling
- **Skin rash in legs** - well-demarcated, erythematous, warm rash, particularly below the knee

What is your concern?

What is wrong with me?

- From what you told me and after I examined you, most likely you have a condition called FMF
- It is a disease run in family, in which there is defect in body own defense system causing soreness - inflammation in joints, covering layers of lungs and in your bowel and causing high body temperature
- What we need to do is to run some blood tests and imaging to confirm our diagnosis and to refer you to chest doctor, bowel doctor and social worker to give you proper plan of management and we will offer family screening if diagnosis is confirmed
- Will give you pain medicine to alleviate your tummy pain
- **Is that okay with you?**
- **Do you have any other concern?**

Examiners' questions:

What are your findings?

What is your diagnosis?

What is FMF?

- Known as **recurrent polyserositis**
- Is an **autosomal recessive** autoinflammatory disorder characterized mainly by brief recurrent episodes of:
    - **Peritonitis**

- **Pleuritis**
- **Arthritis**
- **Fever - preeminent feature**

- FMF occurs within **families**
- Most common in individuals of **Mediterranean descent**

What is the pathophysiology of FMF?

- **Mutations in the MEFV** (Mediterranean fever) gene appear to cause the disease in many cases.
- MEFV produces a **protein called pyrin**.
- The protein is also called **marenostrin**.
- In patients with FMF, **uninhibited pyrin activity** results in **uncontrolled production of (IL-1),** leading to episodes of inflammation (with accompanying fever) in the peritoneum, pleura, and joints.

What is the renal manifestation of FMF?

- **Nephrotic syndrome**
  - **Before** the institution of **colchicine** therapy, mortality due to nephrotic syndrome was almost **universal** by age 50 years

Why this patient had appendectomy?

- Many patients with undiagnosed FMF have undergone appendectomy because the **severity of the peritoneal episodes** seemed to indicate appendicitis.

What are the musculoskeletal complications of FMF?

- **Chronic arthritis**
  - Approximately **5% of patients** with FMF develop **chronic arthritis** that sometimes leads to destructive arthritis of hips or knees and may necessitate joint replacements.
  - Approximately **10% of patients** with chronic arthritis develop **seronegative spondyloarthropathy**.
  - The rate of synovial symptoms varies from 25-75% in reported series.
  - The episodes may resemble gout in their acute onset and intensity.
  - Knees, ankles, and wrists are the joints most affected.

- Arthritic symptoms tend to last several days longer than abdominal symptoms.
- Episodes can be protracted.
- The joints are normal between attacks, and permanent damage is unusual.
- Arthritis may be the only manifestation of FMF.
- The diagnosis of FMF should be considered in patients who have a family history of FMF or live in an endemic area and experience episodes of arthritis.

Any other manifestations of FMF?

- **Fertility and pregnancy:**
  - Approximately **one third** of female patients with FMF are infertile, and 20-30% of pregnancies result in **fetal loss**.
- **Peritoneal symptoms:**
  - Almost all patients with FMF experience abdominal episodes.
  - **Abdominal pain** develops and may progress to **peritonitis**.
  - Frequently the clinical presentation is consistent with **appendicitis** or **cholecystitis**, so patients commonly undergo **appendectomies** and **cholecystectomies**
  - In many cases, patients develop **constipation** during the attack and diarrhea after the attack resolves.
- **Pleural and pericardial symptoms:**
  - The frequency of pleural and pericardial attacks varies among ethnic groups, with 25-80% of patients reporting pleuritic episodes.
  - **Effusions** occasionally occur.
  - **Pericarditis** may develop, but **tamponade** and **constrictive pericarditis are rare**
- **Other manifestations:**
  - **Dermatological - Rash**
  - **Vasculitis** - HSP
  - **CNS**- Headache, seizure
  - **Testicular pain**
- **Amyloidosis:**
  - In a patient of the appropriate ethnic group, the typical progression of **amyloidosis** in FMF is **proteinuria**, followed by

nephrotic syndrome, and, inevitably, **death from renal failure**.

- Prolonged survival resulting from colchicine therapy, dialysis, and renal transplantation allows additional manifestations of amyloidosis to develop.
- Some patients have **intestinal involvement**, which may lead to **malabsorption** and **death**.

What are the differential diagnoses of FMF?

1- **Periodic fever syndrome**
2- Acute peritonitis
3- Acute appendicitis
4- Pericarditis
5- Lyme disease
6- SLE

How are you going to investigate this case?

Basic investigations:

- **Elevated acute-phase reactants:**
  - ESR, CRP
  - **Amyloid A protein**
  - **Fibrinogen**
- RFT
- High WBC - during attacks

Urinalysis:

- Proteinuria
- Hematuria 5%

Confirm diagnosis:

- **Genetic Testing:**
  - MEFV gene mutation
- **Imaging Studies:**
  - Air-fluid levels
  - Pleural effusions
  - Synovial effusions
- **Histologic Findings:**
  - Massive amyloid infiltration of blood vessels and the endothelial side of the glomerular basement membrane in kidneys

- **Renal biopsy** or, alternatively, **submucosal rectal biopsy**, is indicated in these patients.

How are you going to treat FMF?

- **Colchicine:**
  - Colchicine is so effective in preventing attacks of (FMF) and preventing the development of amyloidosis
- **Biologics:**
  - In patients whose conditions do not respond to colchicine, biologic therapy-in, agents directed toward (IL-1) may be effective.
  - ↓
    1. **Interferon-alpha**
    2. **TNF–blocking drug etanercept**
    3. **IL-1 receptor antagonists anakinra and rilonacept**
    4. **Canakinumab**
- **Chronic arthritis in a patient with FMF might need additional** medications, such as:
  - DMARDs
  - Intra-articular steroid
  - Biologics

What do you know about colchicine toxicity?

- Is a serious complication that should be given adequate consideration and be prevented
- **Potential causes include:**
  - Exceeding the recommended dose - 3 mg daily for FMF in adults
  - Liver or renal failure
  - Concomitant administration of other drugs metabolized by cytochrome 3A4
- Colchicine should not be discontinued during conception, pregnancy, or lactation

MRCP-PAES

Brief clinical consultation

Fever in the returning traveler

- Your role: you are an **ST2 on the MAU**
- You have been asked to see Mr. Kim Lake, a 52-year-old who has been feeling unwell and **feverish since returning from holiday last** week.
- Your task: to assess the patient's problems and address any questions or concerns raised by him.

Confirmations:

- **Self**
- **Patient**
- **Agenda**

Opening question:

- You are suffering from high body temperature since your return from your holiday, could you elucidate for me more, please?
    - Yes doctor, I have been feeling unwell for the past week or so, with fever, muscle aches and slight headache.
    - The headaches eased after paracetamol, but the fever was particularly bad last night, disturbing my sleep, and I could not go to work today.
    - I attended A&E as my GP is closed this afternoon.

Analysis of complaint:

ODPARA -OCD

- **When** did it start?
- Did you **measure** it?
- Is it coming in **certain time** during the day?
- **How long** it goes?

- Any associated rigor or **sweating** or feeling **unwell**?

- Is it responding to any **medicine** you take?
- Any **neck rigidity**?
- Cough, SOB, heart racing?
- Any loose motion or tummy pain
    - Yes, I have **loose motion**
- Any **slime** or **blood** content
- Easy **flushed**?
- **How many** episodes
- Associated **type of food**
- **Other people** developed same
- Did you **dine out** during travel – any **street food**?
- Any joint pain or skin rash?
- Any burning during peeing?

Past Medical History:

- Transfusions
- Surgeries

Family history:

Drug History:

- Medication list
- Allergies

Social History:

- What you do for living?
- **Travel** - where?
    - To Gambia, for two weeks
- **Vaccination**
- **Prophylactic medications** - **anti-malarial**, how you took them?
    - Expensive
    - I did not take them
- **Accommodation**
- **Food**
- **Water sources**
- Swimming
- **Sexual encounters** - detailed
- Tattooing, piercing

- Insects, animals' exposure
- Smoking
- Alcohol

Can I examine you?

- **Observation chart**
- General look, pallor, jaundice
- **Lymphadenopathy**
- **Rashes, insects' bites**
- Chest
- CVS
- Abdominal examination:
    - Hepatosplenomegaly
- **Genital area:**
    - Inguinal LAP
- **Skin- rash, any wound**

What is your concern?

What is wrong with me?

- From what you told me and after I examined you, the cause for your high body temperature and feeling unwell is most likely an infection caught whilst abroad.
- We are going to send off tests.
- Will give some medicine for high body temperature
- Depending on results we can advise on whether you need to come into hospital and have the medication.
- We will stop the chemoprophylaxis on admission to hospital as this may interfere with parasite detection.
- Malaria prophylaxis may delay the onset of symptoms and obscure the microscopic diagnosis.
- **Is that okay with you?**

Should I have taken the antimalarials?

- We do advise taking the antimalaria tablets to reduce the risk of malaria which can be a serious infection and can be life-threatening.
- Let us focus on finding and treating what is making you unwell now, and we can deal with future travel later.

Do I have to stay in hospital? I have got a big contract coming up.

- I would advise waiting until the results are back, and I can then explain the plan including whether we would advise you to stay in hospital based on these results.

Examiners' questions:

What are your findings?

What is your diagnosis?

What are the differential diagnoses?

1- **Malaria**
   - 40% may not have fever at presentation
   - Examination can be normal
   - Differential diagnoses include other

2- **Other travel-associated infections:**
   - typhoid fever
   - hepatitis, dengue fever
   - HIV
   - etc.

How you will investigate this case?

- **Basic blood tests**
  - Malaria may show mild anemia, thrombocytopenia, coagulopathy, and renal impairment
    - FBC, INR
    - U&E, LFT
    - ESR, CRP
- **Blood culture**
- Urine
  - Culture
  - Dipstick - **hemoglobinuria**
- **Stool** for microscopy, culture, cysts, and parasites diarrhoea
- Urgent thick and thin films on three consecutive days

- **Rapid diagnostic testing (RDT) for malaria:**
  - Irrespective of prophylaxis

- **Less sensitive** for non-falciparum malaria as it cannot give the additional information of parasite count, maturity

- **CXR** to rule out community-acquired pneumonia
- **Hepatitis serology** if jaundice or hepatitis changes on liver tests
- **HIV serology**

How you will manage this case?

- **MDT**- ID doctor
- Depends on the results
- If **malaria** confirmed, need to know:
  - **Type**
  - **Parasitemia level**
  - Involve local **microbiology specialists** and/or local infectious diseases referral center to advise on therapy
  - Admit if:
    1- If **falciparum**
    2- **mixed** infection
    3- species **unclear**:
  - **If falciparum:**
    - Need to know **parasite count**
    - As it is one of several criteria which guide management
    - If **severe/complicated falciparum** infection:
      - Involve **critical care** team
      - Consider **admission to ICU**
      - Seek help from specialist **infection/ tropical medicine unit**.
      - Give **oxygen**.
      - Careful **fluid balance**.
      - Monitor blood **glucose** closely.
      - **ECG** monitoring: Particularly during **quinine** IV
      - **4 hourly observation** including **GCS**.
      - Daily FBC, INR, U&E, LFT, parasite count.
      - If shock, treat for **gram-negative sepsis**
    - If **complicated falciparum** or patient **vomiting**:
      - **IV quinine** loading dose, then 8 hourly
      - po **doxycycline** or **artesunate**

    - If **uncomplicated falciparum**:
        - **Oral** treatment
    - **If non-falciparum malaria - vivax, ovale, malariae:**
        - **Outpatient therapy** is usually appropriate depending on clinical judgement, availability of follow-up, etc.
- Adherence to antimalarials does not exclude malaria
- Notify all cases to local Health Protection Agency

How would you assess the severity of malaria?

- Using the **British Infection Society (BIS) criteria** for malaria below:
- Major features of severe or complicated falciparum malaria (as per BIS guidelines) = one or more of:
    - Impaired **consciousness** or **seizures**
    - **Hypoglycemia**
    - **Parasite count =/> 2%** (lower counts do not exclude severe malaria)
    - **Hemoglobin =/> 8 g/dL**
    - Spontaneous **bleeding/DIC**
    - **Hemoglobinuria (without G6PD)**
    - **Renal impairment** or electrolyte acid–base disturbance (pH <7.3)
    - **Pulmonary oedema** or **ARDS**
    - **Shock** (BP <90/60) (algid malaria) may be due to gram-negative bacteremia

What are the possible complications of severe 'complicated' malaria?

- **Cerebral malaria:**
    - Altered LOC
    - Coma
    - ? Seizures
- **Hypoglycemia**
- **ARDS** / non-cardiogenic pulmonary **oedema**
- **Shock** / circulatory collapse (**algid malaria**)
- **Metabolic acidosis**
- **Acute kidney injury;** fluid and electrolyte abnormalities

- **Hepatic dysfunction:**
    - Jaundice due to hemolysis
    - Cholestasis due to falciparum
- **Coagulopathy +/− DIC**
- **Severe anemia** or massive intravascular **hemolysis**; **hemoglobinuria** (‘blackwater fever’)
- **Sepsis from other sources** (e.g. Gram-negative sepsis causing marked hypotension / shock)
- **Splenic rupture – falciparum**

Why check for 6GP deficiency if primaquine is being considered as treatment for non-falciparum malaria?

- **G6PDD** has been shown to **offer protection** against severe life-threatening infection in these individuals, but drug treatment with **primaquine** in these individuals can cause **severe hemolytic anemia**

MRCP-PACES

Brief Clinical Consultation

Chronic Tophaceous Gout

You are a **doctor in the clinic**
This 84-year-old man has been experiencing **recurrent attacks of pain** in his **forefinger**.
Please take a brief history and focused examination.
Report your findings to the patient and tell him about your management plan.

Gout can present as:

- **Acute –monoarthritis/oligoarthritic**
  - Big toe pain
  - Knee pain
- **Chronic tophaceous gout**
  - Painful swellings in elbow and lobe of ear

Opening question:

- You have been troubled with pain in your forefingers
- Could you tell me more about that?

Analysis of foot pain:

SONE:

- **Site**
  - Where the pain exactly?
    - In all joints of my hands
  - Anywhere else pain?
- **Onset**
  - Sudden
  - Gradual
- **Exacerbation and relieving factors:**
  - Increased by movement
  - Improved by rest
- **Stiffness** – If no stiffness → mechanical
- **Functional status** – any difficulty with your hand?

- **Diurnal variation in attacks:**
    - Any **time of the day** the pain getting more?
    - The **beginning** of a **flare** of gout usually commences in the **middle of the night** or in the **early morning**.
- **Color change of joints**
- Any **focus of bug infection** anywhere in your body?
- **Association:**
    - **Hypertension**
    - DM
    - Diabetes insipidus
    - **IHD**
    - Drugs – **diuretics** (especially **thiazides**), **ethambutol**, nicotinic acid, cyclosporine
    - Chronic renal failure
    - Alcoholism
    - **Obesity**
    - **Hypothyroidism**
    - **Hyperparathyroidism**
    - **Myeloproliferative** and/or **lymphoproliferative** disorders
    - **Polycythaemia rubra vera**
    - **Psoriasis**
    - Hyperlipidaemia
    - **Excess purine ingestion** e.g. shellfish, oily fish, legumes
    - **Haemorrhage**
    - Dehydration.
- **Complication**
    - **Urolithiasis -** Urate stones/nephropathy: nephrectomy scars
    - **Urate nephropathy** - Passing Gravels with Urine?
    - **Carpal tunnel syndrome**
- **Alarm symptoms –** high body temperature, weight loss, pumps, and lumps

Differential diagnoses of gout:

DHL mnemonic

- D
    - **Diet**, balanced, sea food?
    - **Drugs**, dose, how long

        - Example thiazide for HTN, aspirin,
        - Ethambutol, pyrazinamide
        - Immune suppression
    - **Disease: psoriasis**
    - Deterioration in kidney function
        - Frothy urine
- H
    - High blood pressure
    - High blood sugar
    - High cholesterol
    - History of smoking and alcohol
- L
- Lumps and pumps
    - Lymphoproliferative diseases

PMH:

- Obesity
- Cancer – lymphoma
- Chemotherapy
- CKD
- HTN

Dietary history:

- Diet rich in purine?

Family history:

Social history:

- Job
- **QOL** – how symptoms affecting you in daily life and at work
- Alcohol – excess associate gout mainly red wine
- Smoking
    - **I advise you to stop smoking and alcohol**
- **Cosmetic concern**

Drug history:

- Allergies
- Medication list
    - **Drugs that increase urate level:**

Endurance

- **Thiazide** diuretics
- Low-dose aspirin
- Theophylline
- **Ciclosporin**
- Levodopa
- **Ethambutol**

Drugs that decrease urate level:

- **Losartan**
- **Fenofibrate**

Can I examine you?

- **Look to site of pain in hands**
- **Acute attack:**
  - **Acutely inflamed joints**
  - **Erythematous** and **tender**
  - **Overlying shiny**
  - **Desquamating skin**.

  Hands:
  - **Asymmetrical** bony swelling affecting the small joints of the hands and feet
  - Typically, gouty arthritis of the hands has an **asymmetrical** distribution.
  - **Deformity**
    - There is asymmetrical deformity and swelling of the small joints of the hand
    - With a history of recurrent attacks, some joints may display these acute signs, whilst others show more chronic tophaceous changes.
  - **Reduced movement and function**
- **Look for olecranon bursitis.**
- **Inspect ulceration carefully:**
  - Tophi may ulcerate **extruding white chalk-like monosodium urate crystals**.
  - **Previous ulceration** and extrusion of crystals from tophi may leave **scars and sinus formation.**

  Tophi
  - There is tophi formation - in the periarticular tissues

Endeavance

- They are **visible** or **palpable**, hard calcified but are **not usually tender**
- **Typical sites are**
  - Ear pinnae- helix
  - Tendon sheath
  - Hands
  - Feet
  - The ulnar surface of the forearm
  - **Achilles tendon**
  - **Olecranon bursa**
  - **Prepatellar bursa**
  - Other pressure points
- Rarely, tophi have been reported to cause - examine for:
  - Carpal tunnel syndrome
  - Cardiac conduction defect
  - Valvular abnormalities

- **Large tophi** may have areas of **necrotic skin** overlying them and may **exude chalky or pasty material** containing **monosodium urate crystals**.
- **Sinuses** may form.

- Look at a **temperature chart**, as gout may be accompanied by a **low-grade pyrexia.**
- **Measure the BP:** gout can lead to **renal impairment** and **renal** impairment itself, the most common **predisposing factor for gout**, may **result in hypertension**.
- **Note:**
  - Alternatively, the patient may have only chronic changes, or indeed, **no overt signs of gout**.

What is your concern?

What is the cause of my hand pain?

- From what you told me and after examining you, most likely you have a disease called **chronic tophaceous gout**.
- This occurs when salt crystals called urate crystals deposits and form nodules around joints.
- The most common sites for tophi are the ears, hands, toes, and knees.

- Tophaceous gout is the consequence of chronic, poorly controlled disease called gout.
- That is why we need to do some laboratory investigations and imaging to confirm the diagnosis and to rule out others
- Will give you some pain medications to ease you pain
- Will refer you to group of specialists including joint doctor, dietician, physiotherapist, and occupational therapist for the best plan of management
- I need you to advise you to stop alcohol and smoking
- **Is that okay with you?**
- **Do you have any other concern?**

Can this be treated effectively?

- Gout can, however, be successfully managed due to effective medications

Can I avoid medication if I alter my diet/lifestyle?

- Dietary factors may account for up to 15 % of the body's serum urate.
- Alcohol increases the synthesis of urate by accelerating the degradation of ATP and decreases the renal excretion of urate by increasing the production of lactic acid

Will I have to take medication for the rest of my life?

- **Lifestyle modifications** are **important,** but most patients will require urate-lowering medication for the **rest of their lives.**
- **Tophi will only resolve if the serum urate is reduced to the lower limit** of the normal range, or a synthetic uricase is administered (**humans and Dalmatians lack the uricase enzyme**).

Will my children develop this disease?'

- **Inherited causes of gout** are **vanishingly rare** and therefore patients' children can be reassured.

What are your positive findings?

1. **Gouty tophi** in forearm, hands and feet and ear pinnae
2. **Joint deformity**

What is the differential diagnosis of the causes of gout?

DHL

1. **Drug**, thiazide
2. **Diet** rich in purine
3. **High** BP, blood sugar, cholesterol - metabolic syndrome

4. **L** - lumps, lymphoproliferative disorders

What are the differential diagnoses of monoarthritis?

What are your differential diagnoses?

1. **Chronic tophaceous gout**
2. **Rheumatoid arthritis**

How you will investigate this case?

- **Basic investigation:**
  - CRP, ESR
  - CBC
  - RFT
  - Uric acid
- **Blood culture**
- **Serology**- borrelia if suspected
- **Urate**
  - Not useful in diagnosis
  - May be normal in acute attack
- **Joint aspirate:**
  - Negative birefringent needle shaped MSU crystals
  - High neutrophils count
  - G stain, better culture
- **Radiology:**
  - **X ray:**
  - **Radiographs of the symptomatic joints:**
    - **Punched out lateral erosions with sclerotic margins** and overhanging edges (‘**mouse-bite erosions’**).
    - The **joint space is preserved** until **late in the disease**.
    - **No juxta-articular osteopenia** (c.f. other inflammatory arthritis)
    - May look like RA findings but:
      1. Punched out erosions
      2. Sclerotic margin
      3. Away from joint not like RA
      4. No periarticular osteopenia or reduced joint space in gout

eminence

What are the risk factors for gout?

- **Increased urate production:**
  - High purine diet- beer, sea food, meat
  - Lymphoproliferative disorders
  - Chronic inflammatory disorders- psoriasis
  - Obesity
  - Drugs- chemo
  - TLS
- **Reduced uric acid excretion:**
  - **Dehydration**
  - **Starvation**
  - CKD
  - **Lactic acidosis**
  - **Ketoacidosis**
  - HTN
  - Drugs: low dose aspirin, ACEI, diuretics, cyclosporine, pyrazinamide

How are going to manage this case?

- **Nonpharmacological**
  - Education and counseling about disease
  - Stop smoking and alcohol
- **Acute attack**
  - **Treat the cause**
  - **Hydration**
  - **NSAIDS**
    - NSAIDs should be avoided in patients with renal insufficiency, recent gastrointestinal (GI) ulceration/bleeding or severe heart failure.
    - **Avoid aspirin** as it causes **uric acid retention** unless given in high doses.
  - **Oral colchicine**
    - Effective but can cause **nausea**, **diarrhoea** or **abdominal pain**
    - First-line treatments.
  - **Steroids**
    - Intra-articular injection of a corticosteroid
    - Short course of systemic corticosteroids

- **Allopurinol or uricosuric drugs** - **probenecid**, **sulphinpyrazone**
  - Should not be started **until the acute attack** has **settled for 2–3 weeks**
  - They can prolong the acute attack or trigger further episodes.

- **Long-term treatment**
  - **Prevention:**
    - **Avoid precipitants**
    - **Allopurinol** (xanthine oxidase inhibitor)
    - **Allopurinol**, a xanthine oxidase inhibitor, is used to **maintain remission** in those patients experiencing **severe** or **recurrent bouts** of disabling **gout**.
  - **Prolonged administration of drugs** that lower the serum urate level should be **considered** following complete resolution of the acute attack when:
    1. there is associated **renal disease**
    2. there have been **recurrent attacks (>3/year)**
    3. there is evidence of **tophi** or **chronic gouty arthritis**
    4. the **patient is young** with a **high serum uric acid** and a **family history** of **renal or heart disease**
    5. **normal levels of serum uric acid cannot be achieved** by **lifestyle** modifications (gradual weight loss and restriction of intake of alcohol and food with a high purine content).

- **Welfare:**
  - QOL
  - Lifestyle modification
  - Pain control
  - Physiotherapy
  - Occupational therapy
  - Exclude septic arthritis

What are the causes of bursitis?

- The most **common causes of bursitis** are **repetitive** use and **trauma**.
- **Systemic causes include**
  1. **Gout**
  2. **Pseudogout**

3. **Rheumatoid arthritis**
4. **Uremia**
5. **hypertrophic pulmonary osteoarthropathy**
6. **infections** such as **tuberculosis**

- **Joint mobility** is usually **preserved** since the **bursae** are **not continuous with the joint space**.
- **Aspiration** and **analysis of bursal fluid** will distinguish septic and crystal bursitis.

What is the differential diagnosis of a single, inflamed joint?

1. **Septic arthritis**-gonococcal or non-gonococcal
2. **Crystal arthritis**-gout or pseudogout
3. **Spondylarthritis**
4. **Mycobacterial or fungal** infection
5. **Osteoarthritis**
6. **Systemic conditions** e.g.
    - **Still's** disease
    - **rheumatic fever**
    - **Lyme** disease

How would you assess a patient with monoarthritis?

- **Septic arthritis must be considered** in every patient with monoarthritis.
- The history does not reliably distinguish between causes of monoarthritis; however, the following features must be asked about

---

- **Onset**-an **insidious** onset is inconsistent with acute gout or bacterial arthritis, but **atypical infection**, **chronic gout**, and **spondyloarthropathy** must be considered
- **Fever**-may occurs in **infection**, **crystal arthritis**, and systemic conditions such as **Still's** disease and **rheumatic fever**.
- **Previous joint disease**-may suggest the diagnosis, put chronic injury leaves the joint susceptible to infection. **Recent steroid injection** is also a **risk factor** for infection.
- **History of trauma**.
- **Distribution**-**gout** typically affects the great toe, whereas **pseudogout** affects the **knee, wrist**, and **shoulder**. However, **infection** and **systemic conditions** may affect any joint.

- **Symptoms of systemic rheumatic disease**-fatigue, rash, sicca symptoms, alopecia, oral ulceration, eye symptoms, Raynaud's phenomenon.
- **Associated features-genitourinary** symptoms or recent sexual exposures may suggest a **reactive** or **gonococcal arthritis**. **Gastrointestinal** symptoms suggest arthritis due to recent **enteric infection** or **inflammatory bowel disease**.
- **Recent travel**- to areas endemic for **Lyme** disease (New Forest-Northeastern United States) and for **tuberculosis**.
- **Predisposing factors**- for **gout** (renal failure, recent chemotherapy, hypertension treatment) and **pseudogout** (haemochromatosis, hypothyroidism. hyperparathyroidism).

- Patients with a clinical suspicion of **septic arthritis** must have **urgent joint aspiration** performed for diagnosis.
- **Septic arthritis** typically causes a **large effusion** and **decreased range of movement**, although these may be **absent if** the patient is **immunosuppressed** or the joint is **prosthetic**.

How are you going to investigate monoarthritis?

Joint aspiration:

- **Leucocyte count, gram stain**, and **culture**
- **Polarized light microscopy** - The crystals can be detected using **spectrophotometry** examination of the joint aspirate.
- **Blood cultures** (if septic arthritis is suspected)
- Rectal, cervical, urethral, pharyngeal, and skin lesion cultures (may reveal gonococcus)

What is the role of serum uric acid levels in the diagnosis of acute gout?

- **Measurement of serum uric acid** levels are **of little use** to diagnose **acute gout**, since values **may be normal in an acute attack**, and conversely asymptomatic hyperuricaemia is relatively common and may co-exist with other causes of monoarthritis.

What is the pathophysiology of gout?

- **Uric acid is produced by the breakdown of purines** in the **liver** by the enzyme **xanthine oxidase**.

- The plasma concentration of uric acid is determined by purine concentration (from diet, breakdown of cellular nucleoproteins, and de novo synthesis), xanthine oxidase activity, and uric acid elimination by the kidneys and gastrointestinal tract.
- **Hyperuricaemia** may occur due to **decreased renal uric acid elimination** or **increased purine production**:

Decreased uric acid excretion	Increased purine production
1. **Idiopathic** - **primary** hyperuricaemia	1. **Idiopathic**
2. **Hypertension**	2. **Lymphoproliferative** and **myeloproliferative** disorders
3. **Increased levels of organic acids** (exercise, **alcohol**, starvation, ketoacidosis)	3. **Chemotherapeutic** drugs
4. **Chronic renal disease**	4. **Secondary polycythemia**
5. **Dehydration**	5. **Severe exfoliative dermatitis**
6. **Drugs:** **Diuretics** **ACE inhibitors** **Aspirin** (low dose) **Ciclosporin, tacrolimus** Pyrazinamide	6. **Glycogen storage diseases**

- The serum uric acid concentration is the major determinant of the risk of developing gout.
- **Diets rich in meat and seafood** increase the risk of developing gout by 50%, although diets containing **purine-rich vegetables** do **not carry the same risk**, and diets containing dairy products are associated with a reduced risk of gout due to the **uricosuric effect of dairy proteins**.
- **Acute attacks may be provoked by**

        - **Dietary excess**
        - **Alcohol**
        - **Systemic illness**
        - Physical **exercise**
        - Drugs (see table above)
        - Initiation of **uricosuric therapy** or a **xanthine oxidase inhibitor** (since acute changes in serum urate can cause arthritis).
- The precipitation of monosodium urate crystals in joints causes inflammation and arthritis.

What is the treatment of acute gout?

- Principles of management of gout include
    - **Symptom control**
    - **Measures to induce remission**
    - **Maintain remission**.
- **Rest**
- **Rehydration**
- **Colchicine** or **short course of steroid** for control of the acute attack.
    - **Colchicine** is an **alternative** if **NSAIDs** are contraindicated due to gastrointestinal or renal disease.
    - Symptom control is with n**on-steroidal anti-inflammatory agents** with colchicine to reduce inflammation.
    - However, nausea, diarrhoea, and abdominal pain are common side-effects
    - **Intra-articular corticosteroid** injection if symptoms persist
- **NSAIDs**
    - **Aspirin should be avoided** since it **decreases uric acid elimination unless** given in **high dose**
- Avoid starting allopurinol or uricosuric drugs during an acute attack and avoid diuretics if possible.
- If blood pressure treatment is required, **losartan is the agent of choice** since it has **uricosuric effects**.

What is the treatment for recurrent gout?

- Patients with recurrent attacks of gout: tophaceous gout, or risk factors for recurrent attacks (renal failure, family history of gout, or metabolic disease) should receive drug therapy to lower serum urate.

- Asymptomatic hyperuricaemia does not require therapy in the absence of a history of gout.
- **Lifestyle measures**
  - **reduce alcohol**
  - reduce meat intake
  - **lose weight** if obese.
- **Allopurinol**
  - a **xanthine oxidase inhibitor**
  - is the **drug of choice** because of convenience and low incidence of side-effects.
  - An **NSAID or colchicine** should be prescribed **during initiation** of **allopurinol**, for **prophylaxis against an acute attack** of gout
  - **Allopurinol** is relatively **contraindicated** in patients on **azathioprine**, due to the risk of **serious bone marrow suppression**.
  - **Dose reduction** is required in **renal disease**
  - A **uricosuric agent** such as **probenecid** or **benzbromarone** may be used as an **alternative to allopurinol.**
  - **Allopurinol** is prescribed for **prophylaxis** in the following **indications**:

    1. If there are **significantly frequent attacks** i.e. **> 3 per year**.
    2. Presence of **erosions**.
    3. Presence of **tophi**.
    4. **Renal impairment** secondary to sodium urate kidney stones.

  - **Allopurinol should not be commenced during an acute attack**, as it will **prolong the attack**, but there is no need for allopurinol to be discontinued during an attack.
  - **Sulphinpyrazone** and **probenecid** are **rarely used** due to their **side effect profile**.
  - **Febuxostat**, a new **powerful xanthine oxidase inhibitor**, is usually used if there is **insufficient response** or **intolerance** to **allopurinol**.
  - **Benzbromarone**, a **uricosuric drug**, may be used in the presence of **significant renal impairment** on a named-patient basis.

- **In severe cases synthetic uricase are used by monthly IV infusion** and **IL-1 antagonists** can be employed **intermittently** for **severe flares unresponsive to other treatments**.

What is 'pseudogout'?

- Pseudogout is a **crystal arthropathy**, caused by **calcium pyrophosphate crystal deposition**.
- The crystals are **positively birefringent** in polarized light unlike **uric acid crystals** which are **negatively birefringent.**
- Like gout, the **most common presentation is mono/oligo-arthritis**.
- However, the **knee is the most frequently involved** joint in **pseudogout,** unlike **gout which most commonly affects the great toe**.
- The **radiographic appearance of pseudogout is chondrocalcinosis**, due to **pyrophosphate crystal** deposition on **articular cartilage**.
- **Clinical associations are**

1. Haemochromatosis
2. Hypothyroidism
3. Chronic renal failure
4. **Hyperparathyroidism**
5. **Familial hypocalciuric hypercalcemia**.

	Gout	Pseudogout
Crystals	**Negatively birefringent urate** crystals	**Positively birefringent pyrophosphate** crystals
Distribution	**Monoarticular**: **1st MTP**, **ankle, knee**	**Oligoarticular**: **knee**, **wrist**
Associations	**Hyperuricaemia**, chronic **renal failure**, **drugs**	**Haemochromatosis**, **hypothyroidism**, **chronic renal failure**

What are the renal manifestations of hyperuricaemia?

- **Urolithiasis**
  - uric acid stones comprise **less than 10% of all renal stones**, and affect **less than 10% of-patients with gout**
  - Uric acid stones are **not radiopaque**, hence **plain X-rays** are **unhelpful** in diagnosis.

- Treatment involves **hydration, alkalinization** of the urine with **potassium bicarbonate or potassium citrate**, to **dissolve stones**, and **allopurinol**.

- **Chronic urate nephropathy**
  - Typically causes mild renal impairment due to renal **tubular obstruction** from uric acid crystals.
- **Acute crystal nephropathy**
  - Is a form of acute renal failure, due to precipitation of uric acid crystals within the collecting ducts.
  - The most common cause is **tumor lysis syndrome**
  - Patients develop hyperphosphataemia, hyperuricaemia, hypocalcemia (due to **precipitation of calcium phosphate**), and hyperkalemia.
  - **Allopurinol** is used for **prophylaxis** during chemotherapy, along with **hydration** and **alkalinization** of the urine.
  - **Recombinant Aspergillus uricase (Rasburicase)** is used for treatment.

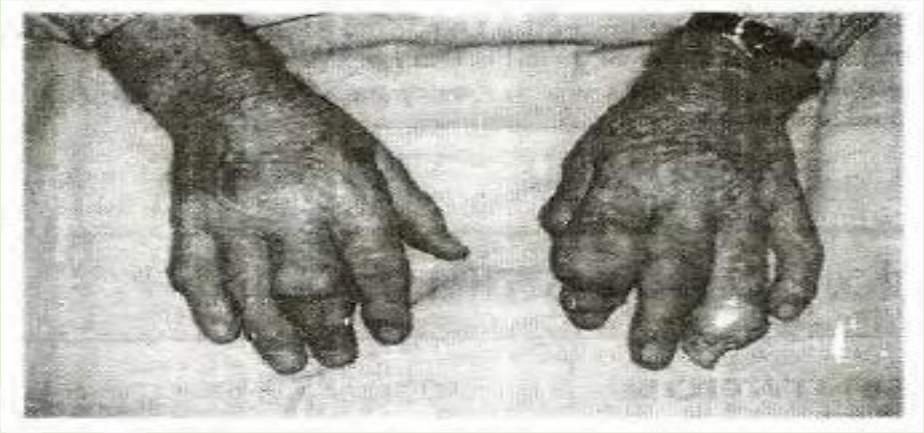


Figure 111.1

- In **chronic tophaceous gout**, the **tophi** can sometimes be clinically **indistinguishable from rheumatoid nodules**, although they may appear as **eccentric swellings.**

Which are the common infective causes of arthritis?

- **Bacterial (non-gonococcal) arthritis:**
  - The most common route of infection is through **haematogenous** spread.

- Predisposing factors are advanced age, prosthetic joints, pre-existing arthritis, intravenous drug use, indwelling venous catheters, and immunocompromised states.
- Staphylococci are the most common organism causing septic arthritis and osteomyelitis in adults.
- **Staph aureus** typically infects **native joints**, whereas **Staph epidermidis** infects **prosthetic joints.**
- **Streptococci** may cause joint infection in patients with **splenic dysfunction**, or with another source of streptococcal infection, such as infective endocarditis.
- **Group A streptococci** (e.g. Strep. pyogenes. Strep pneumoniae) are causative agents of rheumatic fever, although the associated **arthritis** is **immune-mediated**~ polyarticular and migratory **rather than infective.**

- **Gonococcal arthritis:**
  - Arthritis is a manifestation of **disseminated gonococcal infection**.
  - Patients typically present with **purulent arthritis** which **may affect more than one joint**, or a **triad** of **dermatitis, tenosynovitis**, and **polyarthralgia** without purulent arthritis.
  - **Gonococcus** may be identified **from blood cultures** from **synovial fluid**, or from **skin, pharyngeal, cervical, urethral, and rectal swabs.**
- **Mycobacterial arthritis**:
  - M. tuberculosis and M. leprae can cause suppurative bone and joint infection.
  - Furthermore, tuberculosis is associated with a reactive tenosynovitis and arthritis, termed **Poncet's disease**, developing in the presence of active tuberculosis elsewhere.
- **Lyme disease**:
  - Arthritis is a late complication of Lyme disease.
  - The initial infection with **Borrelia burgdorferi** is through a bite from an infected tick.
  - Early disease is characterized by the rash of **erythema chronicum migrans**, followed by late **cardiac**, **neurological** and **rheumatological** manifestations.

- In the USA, 60% of patients develop **acute monoarthritis** or **oligoarthritis**, although Lyme arthritis is less common in Europe.

- **Viral arthritis:**
  - Viral infections which may cause a reactive arthritis are **parvovirus B19, rubella, hepatitis B, and HIV.**

Which medical conditions are associated with under secretion of urate?

- **90 % of patients with gout are under secretors of urate** (and **10 % are over-producers of urate**).
- **The following conditions are associated with under-secretion:**
  - **Renal disease** (including polycystic kidney disease, **lead nephropathy** (**saturnine gout**))
  - **Ketoacidosis/lactic acidosis**
  - **Respiratory acidosis**
  - **Hyperparathyroidism**
  - **Hypothyroidism**

What is the mechanism of action of allopurinol and why is not helpful in an acute attack of gout?

- **Allopurinol inhibits the enzyme xanthine oxidase** that catalyses the **conversion of hypoxanthine to xanthine** and xanthine in turn **to uric acid**.
- It is an **analogue of hypoxanthine** and inhibits the enzyme by substrate competition.
- **Allopurinol is converted to alloxanthine by xanthine oxidase** and this metabolite is an effective non-competitive inhibitor of the enzyme.
- The **pharmacological action** of allopurinol is **largely due to alloxanthine**.
- The result of the **action of allopurinol** is that the concentration of **insoluble urates** in tissues, plasma and urine **decreases** while that of the **more soluble xanthines and hypoxathines increases**.
- **Hypoxanthine and xanthine are in turn converted into adenosine** and **guanosine monophosphates** that cause feedback inhibition of amidophosphoribosyl transferase, the first and rate-limiting enzyme of purine biosynthesis.
- **Allopurinol**, therefore, **decreases both uric acid formation and purine synthesis**.

- Initiation of **allopurinol** therapy **may lower serum urate levels rapidly** with the potential for **urate reabsorption from tissue** deposits, **provoking an acute attack of gout**.

What important drug interactions do you know in the management of gout?

Allopurinol and azathioprine:

- **Mercaptopurine**, the active **metabolite of azathioprine**, is normally **metabolized by the xanthine oxidase pathway**.
- By inhibiting this enzyme pathway, allopurinol **increases the effect** of **mercaptopurine** that may result in **toxic bone marrow suppression**.

Allopurinol and warfarin:

- The effect of warfarin is increased due to **inhibition** of its **metabolism**.

Colchicine and statins:

- **Colchicine increases the risk of myopathy** in patients taking lipid-regulating medication.

Colchicine and Ciclosporin:

- The combination may result in nephrotoxicity and/or myopathy.

Who was Podagra?

- She was a daughter of Bacchus (the God of wine) and Aphrodite and was known as the **foot torturer** in classical mythology.

what are 4 stages of gouty arthritis?

1. **Asymptomatic hyperuricaemia**
2. **Acute gouty arthritis**
3. **Inter-critical gout**
4. **Chronic tophaceous gout.**

- As the candidate is most likely to encounter such a patient in the scenario of hand examination the same approach to history, examination, and functional assessment should be taken as outlined for a patient with RA

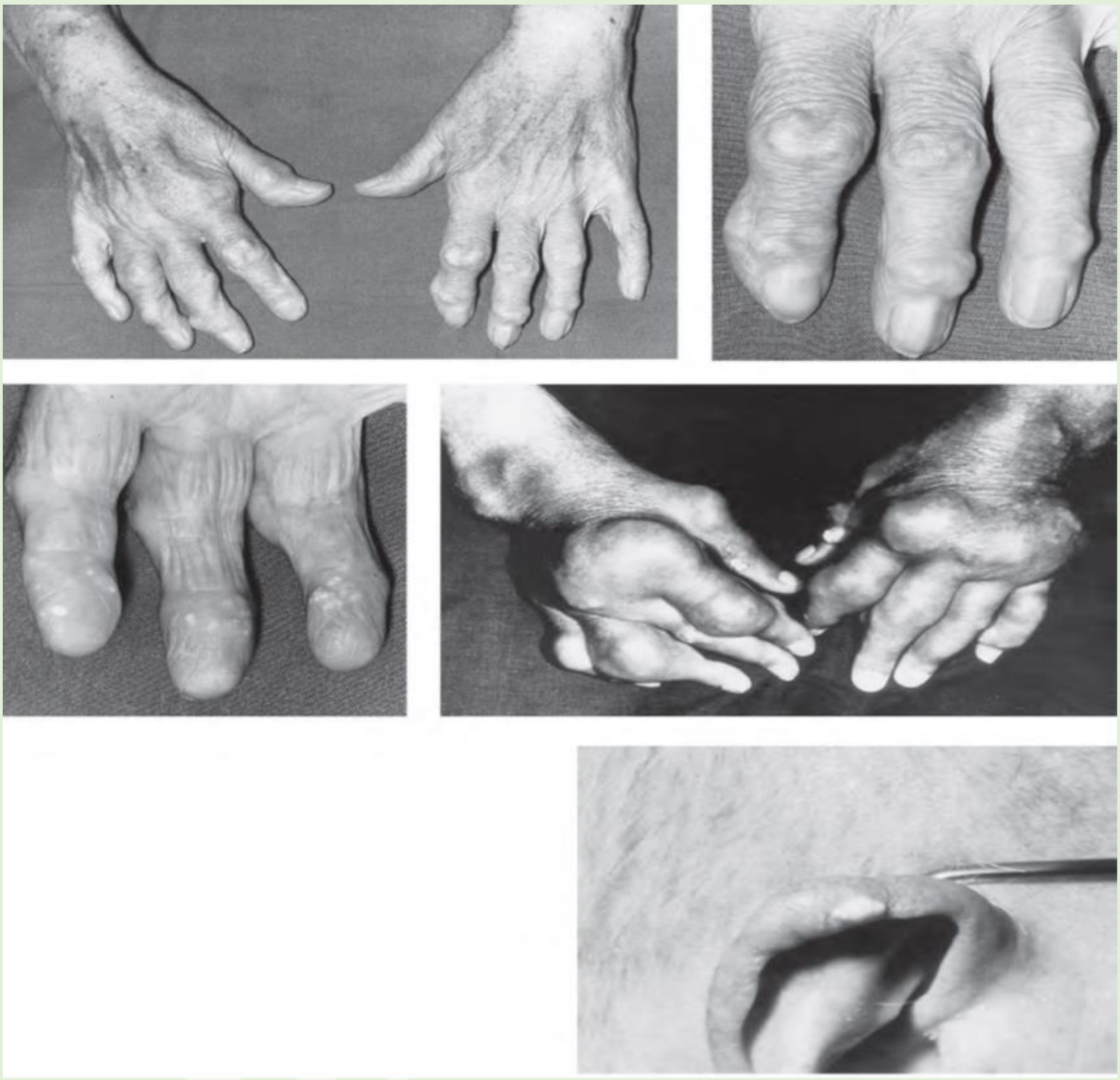


Figure I5.52 (a–d) **Gouty tophi and arthropathy**.
(e) An extreme case of tophaceous gout.
(f) A **tophus** on the **helix of the ear**.

- Chronic tophaceous gout **results from recurrent acute attacks**.
- Tophus formation is **proportional to the severity** and **duration of the disease**.
- However, patients with **severe tophaceous disease** appear to have **milder and less frequent acute attacks** than non-tophaceous patients.

Anecdote

- This man has a **painful knee**.
- Please examine his hands and suggest why.
- He had an **asymmetrical arthropathy** with **gouty tophi**.
- The following **discussion was about gout**, its **management**, **investigations and complications**.

- **Examine the patient's hands.**
- I found the **signs of chronic tophaceous gout**.
- I was then asked about the **management** and treatment of **chronic gout**.

- **227**. I was asked to **examine the hands of a patient**.
- They looked rheumatoid but the patient also seemed to **have tophi**.
- There were no nodules at the elbow and I eventually said it was inactive rheumatoid arthritis.
- One examiner asked what I would think if told that his uric acid was 0.6 mmol/L.
- I said that was because he had gout as well!
- On walking to the next case, they asked me about treatment and I managed to discuss this satisfactorily.

- I was then asked to **look at another man's hands.**
- He had **gouty tophi** but there was nothing on the ears or the elbows.
- They seemed satisfied with this.

- My last short case was another '**Look at this man's hands'** and he was another case of **gouty tophi**.
- The examiners told me that I was correct.
- I was absolutely convinced that I had made an irretrievable mess of the short cases.
- I still cannot understand how they passed me! (Pass)

Endurance
20-12-2018

MRCP-PACES

Brief Clinical Consultation

Gout

You are a doctor in the clinic
Mr. Edwardo is 34 years old, complaining of **severe pain in right foot**

Can present as:

- **Acute –monoarthritis/oligoarthritic**
  - Big toe pain
  - Knee pain
- **Chronic tophaceous gout**
  - Painful swellings in elbow and lobe of ear

Opening question:

- You have been troubled with pain in your right foot
- Could you tell me more about that?

Analysis of foot pain:

SONE:

- **Site**
  - Where the pain exactly?
    - In big toe
    - **Typically, in first MTP joint**
  - Anywhere else pain?
- **Onset**
  - Sudden
  - Gradual
- **Exacerbation and relieving factors:**
    - Increased by movement
    - Improved by rest

- **Mechanical pain:**
  - Increase by movement
  - Improve by rest
- **Inflammatory pain:**

- Increase by rest
- Improve by movement

1. Burn in water work, red eyes: **reactive arthritis**
2. Ankle or neck pain: **ankylosing spondylitis**
3. Change in bowel: **IBD**

- **Stiffness** – If no stiffness → mechanical
- **Functional status** – any difficulty with your foot or knee?
- Any **time of the day** the pain getting more? – more at night
- **Color change**
- Any **focus of bug infection** any where in your body?

Analysis of differential diagnoses:

1. **Trauma**
2. **OA-** obesity
3. **Hemophilia -** Bleeding
4. **pseudogout -** Weight change
5. **Hemochromatosis:** Skin tanning
6. **Septic arthritis:** high body temperature, sweating, body shakes**,** infection else where
7. **Seronegative arthritis:**
    - Rash: **psoriasis**
    - Burn in water work, red eyes: **Reactive arthritis**
    - Ankle or neck pain: **ankylosing spondylitis**
    - Change in bowel: **IBD**
8. **Alarm symptoms –** high body temperature, weight loss, pumps, and lumps

Differential diagnoses of gout:

DHL mnemonic

- **D**
    - **Diet**, balanced, sea food?
    - **Drugs**, dose, how long
        - Example thiazide for HTN, aspirin,
        - Ethambutol, pyrazinamide
        - Immune suppression
    - **Disease: psoriasis**

        - Deterioration in kidney function
            - Frothy urine
    - **H**
        - High blood pressure
        - High blood sugar
        - High cholesterol
        - History of smoking and alcohol
    - **L**
    - Lumps and pumps
        - Lymphoproliferative diseases

PMH:

- Obesity
- Cancer – lymphoma
- Chemotherapy
- CKD
- RRT
- Insulin resistance
- Hypertension
- Chronic inflammatory problems
- Drug history:
- thiazides, chemotherapy

Dietary history:

- Diet rich in purine?

Family history:

Social history:

- Job
- **QOL** – how symptoms affecting you in daily life and at work
- Alcohol – excess associate gout
- Smoking
    - **I advise you to stop smoking and alcohol**
    - Travel history
- **Cosmetic concern**

Drug history:

- Allergies

- Medication list
    - Colchicine
    - NSAIDS

Can I examine you?

- **Look to site of pain**
    - Swellings in the first MCP joint - **podagra**
    - Erythema
    - Warmth, swelling, limitation of movement
    - **Tenderness- beware**
    - Inflamed Heberden's and Bouchard's nodes and bursitis - olecranon, patella
    - **If knee pain:**
        - Inspect:
            - Temperature by dorsum of hand
            - Tenderness
            - Taping for effusion
            - Tightness of synovium
            - Movement:
                - Passive
                - Active, crepitations

Ear lobes for tophi

Joint of hands: Bony swelling = **tophi** , **deformity**

- **Chronic tophaceous gout signs:**
    - Hard, calcified, painless nodules
    - Ear pinnae
    - Hands
    - Feet
    - Ulnar surface of forearm
    - Achilles tendon
- **Sign of CKD**
- LAP
- **Abdomen**- Hepatosplenomegaly
- Pallor, jaundice
- Petechiae
- Fingertips for diabetes
- I would like to check BP, blood sugar and urine for glycosuria

What is your concern?

What is the cause of my knee pain?

- From what you told me and after examining you, most likely you have a disease called gout
- It is a medical term for a medical condition in which there is deposition of some salt crystals inside your knee joint
- Many reasons for that
- That is why we need to do some laboratory investigations and imaging to confirm the diagnosis and to rule out others
- Will give you some pain medications to ease you pain
- Will refer you to group of specialists including joint doctor, dietician, physiotherapist, and occupational therapist for the best plan of management
- I need you to advise you to stop alcohol and smoking
- **Is that okay with you?**
- **Do you have any other concern?**

What are your positive findings?

- Gouty tophi

What the differential diagnosis of knee swelling this patient?

1. Gout
2. Septic arthritis, no fever
3. Psoriasis, no skin rash
4. Pseudogout

What is the differential diagnosis of the causes of gout?

DHL

1. **Drug**, thiazide
2. **Diet** rich in purine
3. **High** BP, blood sugar, cholesterol - metabolic syndrome
4. **L** - lumps, lymphoproliferative disorders

What are the differential diagnoses of monoarthritis?

1. Gout

2. Septic arthritis
3. Pseudogout
4. Osteoarthritis
5. Spondylarthritis
6. Tubercular arthritis

What are your differential diagnoses?

1. Gout:

- Deposition of **monosodium urate crystals**
- In joints, bone, or soft tissue
- By product of purine metabolism in liver by xanthine oxidase
- **Triggers:**
  - Dehydration
  - Starvation
  - Exercise
  - Diet- alcohol
  - Medications

2. Septic arthritis

- **Symptoms:**
  - Fever, rigor? joint disease
- Sexual history
- **Examination**:
  - Hot tender joint
  - Surrounding erythema
- **Investigation:**
  - CBC, ESR, CRP, blood culture
  - Joint aspirate, G stain, culture
  - Usually turbid synovial fluid with high neutrophil count
  - MRI to exclude osteomyelitis
- **TTT:**
  - Emergency antibiotics, before diagnosis
  - Flucloxacillin, gentamicin
  - Ortho referral for arthroscopic joint wash out

3. Pseud-gout:

- **Calcium pyrophosphate crystals**
- Associate hemochromatosis, HPTH
- OA

- Low phosphate, low magnesium
- CKD
- Mono or oligoarthritic
- **Mostly in knees**
- Also, wrist and hip
- **Investigations:**
    - ESR, CRP
    - Xray- chondrocalcinosis which is joint crystal deposition in cartilage
    - Joint aspiration: rhomboidal weakly positive birefringent calcium
    - pyrophosphate crystals on polarized light microscopy
- **TTT:**
    - Self-limiting
    - NSAIDS
    - Colchicine
    - Steroids PO or intra-articular if sepsis excluded
    - Joint aspiration may ease pain

4. **OA:**

- Pain worse on movement
- Ease on rest
- Bony swellings at **distal IPJ - Heberden's nodes**
- **Proximal IPJ - Bouchard's nodes**
- Square appearance of first MCP joint
- Deformities - varus of knee
- Crepitus, locking
- **Gait: antalgic**
- **Trendelenburg's gait if hip affected**
- **Investigations:**
    - **Joint x Ray**
        1. Loss of joint space
        2. Marginal osteophytes
        3. Subchondral sclerosis
        4. Subchondral cysts
    - **Aspiration**
        1. clear fluid
        2. Low WBC

- **TTT:**
  - Intra articular steroid
  - Physiotherapy
  - Occupational therapy
  - Joint replacement

5. **RA**
6. **Seronegative spondyloarthropathy**

How you will investigate this case?

- **Basic investigation:**
  - CRP, ESR
  - CBC
  - RFT
  - Uric acid
- **Blood culture**
- **Serology**- borrelia if suspected
- **Urate**
  - Not useful in diagnosis
  - May be normal in acute attack
- **Joint aspirate:**
  - Negative birefringent needle shaped MSU crystals
  - High neutrophils count
  - G stain, better culture
- **Radiology:**
  - **X ray:**
    - XR punched out bony lesion
    - May look like RA findings
      1. Punched out erosions
      2. Sclerotic margin
      3. Away from joint not like RA
      4. No periarticular osteopenia or reduced joint space in gout

What are the risk factors for gout?

- **Increased urate production:**
  - High purine diet- beer, sea food, meat
  - Lymphoproliferative disorders

- Chronic inflammatory disorders- psoriasis
- Obesity
- Drugs- chemo
- TLS

- **Reduced uric acid excretion:**
  - **Dehydration**
  - **Starvation**
  - CKD
  - **Lactic acidosis**
  - **Ketoacidosis**
  - HTN
  - Drugs: low dose aspirin, ACEI, diuretics, cyclosporine, pyrazinamide

How are going to mange this case?

- **Nonpharmacological**
  - Education and counseling about disease
  - Stop smoking and alcohol
- **Prevention:**
  - Dietary change
  - Stop risk factors
  - Use colchicine and NSAIDS before to prevent acute attack
  - Lifelong treatment
  - **Preventive treatment:**
    - **Allopurinol -** xanthine oxidase inhibitor
      - **Indication:**
        1. More than Two attacks per year
        2. Renal stone
        3. Gouty tophi
      - If contra indicated use uricosuric drugs like probenecid
- **Acute attack? Self-limiting**
- Alternative medicine to water work pill, thiazide by heart doctor
- **Acute attack treatment:**
  - Intra articular steroid
  - The **cause**: ketoacidosis.
  - **Analgesia**:

1. NSAIDS
2. In CKD- **Colchicine**, causes diarrhea
3. **Corticosteroid**- intra articular, exclude sepsis

- **Chronic/recurrent:**
  1. **Allopurinol**
  2. **Febuxostat**
  3. **Probenecid**
- **Welfare:**
  - QOL
  - Lifestyle modification
  - Pain control
  - Physiotherapy
  - Occupational therapy
  - Exclude septic arthritis

MRCP-PACES

Brief clinical consultation

HTN- MEN2A syndrome

Scenarios:

You are **SHO** in endocrinology clinic
Mr. Edwardo is a 30 years old male patient
Complaining of **high blood pressure**

Confirmation:

- Self
- Patient
- Agenda

Opening question:

- You have been troubled with high blood pressure
- **Could you tell me more about that?**
  - Yes doctor, I did routine health check up with my GP and he told me that my blood pressure is high

Analysis of complaint – High blood pressure:

- **What was the last BP reading?**
  - 180/100
- **Is the first time** to have this high blood pressure reading?
- **Symptoms of end organs affection:**
  - **CNS**:
    - Headache, weakness anywhere, Fits, feeling sick
  - **Retinopathy**:
    - eyesight problem, any loss of vision
  - **Heart**:
    - SOB, chest pain, heart acing
  - **Nephropathy**:
    - Change in water work, amount, color, and frequency

- **Compliance of medications**
  - Are you receiving any regular medications?
  - Are you taking them regularly?
- **Secondary causes of HTN:**
  - **White coat HTN:**
    - Do you feel anxious when meet doctor?
  - **Endocrine causes:**
    - **Conn's syndrome**, low potassium, muscle weakness, heart racing
    - **Weight gain:** acromegaly, Cushing's, and hypothyroidism
    - **Weight loss**: **Pheochromocytoma** – **rule of H** - headache, heart racing, handshake, hand sweating, high BP, high blood sugar
  - **Kidney problem:**
    - **APKD**
      - Tummy pain, blood in urine, stones
    - **SLE**
      - joint pain, rash
    - **GN**
    - **Scleroderma renal crisis**
      - Tight skin

Systemic review

Screen for the MEN -2A components:

- **Medullary thyroid carcinoma:**
  - Neck mass
  - **Diarrhoea** due to elevated **calcitonin** levels
- **Pheochromocytoma:**
  - **Tumor of adrenal medulla**
    - Hypertension
    - Episodic sweating
    - Headache
    - Tremor
    - Anxiety
- **Parathyroid hyperplasia:**
  - Features of hypercalcemia

Screen for the differential of the pheochromocytoma:

- **Tuberous sclerosis**
- **Neurofibromatosis**
  - Skin rash
- **von-Hippel Lindau**
  - Change in water work

Drug history:

- Medication list:
  - **NSAIDs**
  - **OCP –** in female
  - **Steroids**
  - Private question – are you taking any Illicit drugs?

Family history:

- **Primary HTN:**
  - Any family member having
- Cancer

Past Medical History:

- Thyroidectomy
- Parathyroidectomy
- HTN
- Renal stones

Can I examine you?

- **Observation chart:**
  - Pulse
  - BP
- Hand sweating
- Neck mass - thyroid nodule
- Neck scar
- Fundoscopy - hypertensive retinopathy

Social history:

- QOL
- Job

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- Alcohol
- Smoking

Addressing concerns:

What is wrong with me, doctor

- From what you told me and after examining you, most likely you have a condition called MEN-2A
- It is a medical term for a rare disease run in family
  It causes tumors in glands in front of your neck- thyroid, parathyroid and gland overlying your kidneys - adrenal glands
- We need to arrange some blood tests and scans of neck and abdomen
- And we will refer you to gland doctor for further investigations and management
- We will refer you to genetic counselling to offer you family screening since this disease runs in family

What are your findings?

- Blood pressure 165/98
- PR 105/ minute
- Thyroid nodule of 4x4 cm

What is your diagnosis:

- **MEN-2A**

What are your differential diagnoses of anxiety in this case?

1. Pheochromocytoma
2. Thyrotoxicosis
3. Simple anxiety neurosis

How you will investigate this case?

- **Basic investigations:**
  - CBC
  - Chemistry including calcium
  - TFT
  - Inflammatory markers

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- **MTC:**
  - ❖ **Calcitonin levels**
  - ❖ **CEA**
  - ❖ US neck
  - − **CT** chest and abdomen for metastatic disease
  - − **Histopathology confirmation**
- **Parathyroid hyperplasia:**
  - − Calcium
  - − PTH level
  - − US neck
- **Pheochromocytoma**
  - 24-hour urinary catecholamines and metanephrines
  - Plasma metanephrines
  - CT/MRI of adrenal glands
  - **MIBG** - meta-iodo-benzyl-guanidine scan

How you will manage this case?

- **Pheochromocytoma:**
  - Alpha blocker followed by b-blocker
  - Surgery
- **MTC:**
  - Thyroidectomy
- **Hyperparathyroidism:**
  - Management of hypercalcemia
  - Surgery
  - Long term monitoring: yearly

What are the hereditary pheochromocytomas syndromes?

1. MEN-2 syndrome
2. von-Hippel-Lindau
3. Neurofibromatosis
4. Tuberous sclerosis

What is the gene defect in MEN -2?

- **Mutation in RET proto-oncogene**

MRCP-PACES

Brief clinical consultation

Hypertension

You are SHO in the clinic
Mrs. Lara is 36 years old female with high blood pressure

Confirmations:

- Self
- Patient
- Agenda

Opening question:

- You got troubled with high blood pressure
- Could you tell me more about it?

Analysis of high BP

- **Is it the first time?**
- What was the last reading
  - ✓ 180/100
- Any weight changes?
  - ✓ **Weight loss** – pheochromocytoma
  - ✓ **Weight gain** – hypothyroidism, Cushing's syndrome
- Nose-bleed

Screen for differential diagnosis of the cause:

- **Essential HTN:**
  - Positive family history - Any family member having high BP
  - Middle aged people
- **Endocrine causes:**
  - **Thyroid disease:**
    - Do you tend to feel the Hot weather more than usual?
    - Excessive sweating?

        - Lose motions?
        - Heart racing?
        - Irritability?
        - Weight loss despite an increased appetite?
        - Any neck swelling?
    - **Pheochromocytoma**
        - Episodic headache
        - Tremor, weight loss, flank pain
        - heart racing, handshake, hand sweating
        - high BP, high sugar
        - MEN 2- NF – vHL syndromes features - renal cell carcinoma, blood on passing urine, pain in loins
    - **Acromegaly – MEN1**
        - Ring & shoes size
        - Do they fit?
        - Excessive sweating
        - Ask about MEN1
    - **PCO**
    - **Cushing's syndrome:**
        - Skin changes, **depression**, new onset DM
        - Weight gain more in the face, tummy & around the neck & back
        - Weakness of shoulders & Hips
        - High Blood sugar
    - **Conn's syndrome:**
        - features of **hypokalemia**
            - weakness, muscle cramps, fatigue
            - heart racing
- **Renovascular:**
    1. **Renal Artery Stenosis**
    2. **ADPKD**
    3. **RCC**
        - HTN-sudden onset
        - Resistant to antihypertensives
        - Tummy pain, blood in urine APKD

        - Stones
        - joint pian rash SLE
        - GN
        - SOB (flash pulmonary edema)
- **Coarctation of aorta**
    - palpitations, cold feet, leg pain, muscle cramps
- **Connective tissue diseases and vasculitis:**
    - Joint pain
    - Tight skin – scleroderma renal crisis
    - Skin rash – SLE
    - **PAN**
- **White coat HTN:**
    - Do you feel anxious when meet doctor
- **Hematological - PCV**
- **Metabolic syndrome**

Symptoms of end organs:

- **Encephalopathy:**
    - Headache, LOC, weakness anywhere, fits, vomiting
- **Retinopathy:**
    - Vision problem, any loss of vision
- **Heart:**
    - SOB, chest pain
- **Nephropathy:**
    - Change water work, amount color frequency
- **Primary HTN:**

Past medical history:

Drug history:

- Steroids, **OCP**, **NSAIDs** for SLE joint pain, steroids, ciclosporin
- Side effects of antihypertensives: bendroflumethiazide (impotence and gout)
- Recreational-cocaine, amphetamine
- **Compliance of medicines**
    - Receive medicine regularly

Family history:

Social history:

- Job – any stress at work?
- Personal- alcohol, smoking
  - Stop smoking
  - Pregnancy
  - Menstrual history

Physical examination:

- **Pulse**
  - Radio radial and radio femoral delay
  - Unequal radial pulses
  - Surgical scar for coarctation repair
- Acromegalic features
- Abdomen – in other cases
  - Palpable kidneys – ADPKD
  - Renal bruit - RAS
- Evidence of connective tissue disease:
  - Rash - SLE
  - Joint deformities
  - Tight shiny skin – scleroderma
- **Target organ damage:**
  - Fundoscopy
  - Heart failure, LVH
  - CNS- stroke
- Features of CKD
- Urine dipstick for proteinuria and hematuria

Summarize to patient:

- High BP
- Features of acromegaly
- Anxious when meet doctor

What is your concern?

Why I have high blood pressure?

- From what you told me and after I examined you, most likely you have high blood pressure related to overgrowth of a gland in your

brain secreting protein giving many features you have and causing your high blood pressure.

- We need to do some blood tests and imaging
- Will refer you to gland doctor and social worker and to dietician
- We need you to adopt healthy lifestyle and to do exercise and to stop smoking and to moderate alcohol intake
- Is that okay with you?

Examiners' questions:

Differential diagnosis

1. **White coat HTN**
2. **Essential HTN**
    - **Primary**
    - **Secondary**
        - **Endocrine**- primary hyperaldosteronism (Conn's syndrome), Cushing syndrome, pheochromocytoma, thyroid dysfunction, acromegaly, congenital adrenal hyperplasia
        - **Renal**- renal artery stenosis, APKD, CKD, GN
        - **Vascular**- coartation of aorta, vasculitis, connective tissue disease (SLE, scleroderma)
        - **OSA**
        - **Drugs**- cocaine, amphetamines
        - **Pregnancy** - pre-eclampsia/eclampsia

How are you going to investigate high blood pressure patient?

Confirmations:

- **Ambulatory BP monitoring:**
    - If Basal 140/90 in clinic
    - Two readings per day for week total
    - 14 readings

Investigate for risk factors:

- Fasting blood sugar and HbA1c
- Lipid profile
- **Renal**

        - function tests
        - US kidneys
        - Urine microscopy
        - **Renovascular HTN- doppler flow US, CT/MR angiography**
        - Doppler US of Renal Arteries = Renal artery stenosis
- **Endocrine**
    - **Acromegaly**
    - **TFT - neck US**
    - **Conn syndrome**
        - **Screening tests**
            - Hypokalemia
            - bicarbonate level (metabolic alkalosis)
            - plasma aldosterone to rennin activity ratio (ARR) when greater than 20-25 is highly suggestive
            - **kaliuretic** (urinary K excretion more than 30 mmol/day
        - **Confirmatory**
            - urinary aldosterone level
            - serum aldosterone level
            - salt loading test
        - **CT scan adrenal gland**
- **Coartation of aorta**
        - CXR, CT angiography
- **ECG**, echocardiogram

How you will treat this patient?

- Management of acromegaly – primary disease
- Lifestyle modification
- Treatment of HTN and its cause
        - ACEIs if < 55 years old
        - CCBs, Diuretics > 55 years old
- Treat target organ damage

MRCP-PACES

Brief clinical consultation

Hypoglycemia

- Mrs. Jane, 35 years old patient with recurrent collapse
  Please see her and advice

Scenario:

- Recurrent dizziness
- Syncopal attack
- Recurrent fall

Analysis of complain:

- **What do mean by fall?**
- **What you were doing before?**
- **What did you felt when you got this?**
  - Sweating
  - Tremor
  - Coldness
  - Feeling hungry
- **B- During attacks:**
- **Rule TIA:**
  - Any weakness
  - Abnormal sensation
  - Any fits
- **C- After attacks:**

  Any injury?

Past Medical History:

- Any significant PMH?
- **Any DM?**
  - If yes, then --------->
    - **How long** you have been diabetic?

        - Is it **controlled**?
        - What is the **last blood sugar reading** test covering last 3 month?
    - **Diet:**
        - Are you getting a balanced diet?
        - Is it restricted?
    - **Deterioration of kidney function:**
        - Any **Kidney disease**?
        - Are you taken enough **fluids**?
        - Any **analgesics**?
        - What about **water work**?
        - Any increase **frequency**?
        - Any **frothy pee**?
        - Any **leg swelling**?
        - Nausea and vomiting
    - **Exercise:**
        - Are you doing excessive exercises?
- **Screen for differential diagnoses:**
    - **Insulinoma**
        - Any weight changes?
        - Is it intentional?
        - Where did you put on weight?
        - Which part of your body?
        - **Screen for MEN1**
            - **Hyperparathyroidism:**
                - Passing stones in pee
                - Heart burn
            - **Pituitary:**
                - Headache of ICP
                - Visual problem
            - **Pancreas:**

- **Insulinoma symptoms**
    - Whipple's triad for insulinoma

1. **Symptoms**: Sweating, feeling cold, palpitations, shaky, blurred vision, and light headedness
2. **Low blood sugar** - < 3 mmol/L
3. Symptoms resolved after replacing sugar

- **Drugs**
  - Insulin
  - Sulphonylureas
- **Renal Failure**
- **Adrenal insufficiency**
  - Sudden withdrawal of steroids
  - Primary adrenal insufficiency

- Dizziness on standing from sitting position
- Tummy pain
- Poor appetite
- Tanning of skin
- Weight loss
- Contact with sick person - TB
- Did you stop any medication recently - steroid

Drug History:

- Any allergies?
- Are you on any medications?
- What drug?
- What is the dose?
- Since when you are on them?
- **Any increased doses recently?**

Family History:

- Any significant illnesses
- Any gland problem runs in family?

Social history:

- What do you do for living?
- Do you smoke?
- Do you drink alcohol?

- Are you driving?
- Stop only in unawareness of hypoglycemia

Can I examine you?

- **Fundoscopy**
- Measure **Blood Sugar**
- **Tips of fingers' pulps** for sugar check markings
- Palmar crease **hyperpigmentation**
- Oral cavity hyperpigmentation
- **BP- postural drop**
- **CNS**
  - Proximal myopathy
  - Peripheral neuropathy
- **If insulinoma:**
  - Overweight - BMI
- **If acromegaly:**
  - CTS
  - Bitemporal hemianopia
- **Examination for Signs of renal failure:**
  - Uremic froth
  - Lower limb edema
- **Two minutes warning:**

What is your concern?

What is wrong with me doctor?

- From what you told me and after I examined you, most likely you have a low blood sugar , it is related to problem called MEN-1 affecting many glands in your body including one in your brain called pituitary gland , one infront of your neck called thyroid and one inside your abdomen, called pancreas
- These glands secrete proteins essential for function of your body
- Increase secretion of protein from gland inside abdomen, called insulin is the cause of your low blood sugar level
- What we need to do now is to request some blood tests and to do some imaging, to confirm diagnosis and to rule out others
- We need to admit you for observation while waiting for tests' results
- **Is that okay with you?**

Examiners' questions:

What are your findings in this case?

- This lady with blood sugar check markings at fingers' pulps
- Postural blood pressure drops
- Looks overweight, likely with high BMI
- There are striae in abdominal wall

What is your diagnosis?

- Recurrent hypoglycemia due to insulinoma

What are your differential diagnoses?

- **Drugs:**
  - ❖ Insulin
  - ❖ Sulphonylureas
- **Diet**
  - ❖ Restricted – less eating and drinking
- **Disease**
  - ❖ Addison's disease
- **Deterioration of kidney function**

How you will investigate this case?

- **Basic investigations:**
  - ✓ CBC
  - ✓ Chemistry, including RFT
- **Insulinoma:**
  - ¦ Low insulin level
  - ¦ **High C peptide level**
  - ¦ Observed prolonged fasting
- **Sulphonylureas:**
  - High insulin
  - **Normal C peptide level**
  - Urinary Sulphonylureas
- **Pituitary:**
  - ¦ MRI Brain
- **Addison's:**
  - ¦ Short synacthen test

- Electrolytes - above
- **Associated polyglandular diseases:**
  - Thyroid - TFT, US neck
  - PTH

How you will manage this case?

- Referral to **MDT** including gland doctor and dietician
- Treatment of the **underlying cause**
- **Reduce** insulin or OHM **dose**
- **Dextrose** iv fluid
- **Addison's disease:**
  - Steroid replacement
- **Insulinoma:**
  - Surgery
  - Chemotherapy - streptozotocin
  - mTOR - everolimus

What are the causes of hypoglycemia unawareness in diabetic patients?

1. **Beta Blockers**
2. **Autonomic** Neuropathy
3. **Tightly** controlled blood sugar
4. **Diabetes** for long time
5. **Stress**
6. **Depression**
7. Consuming **alcohol**

Advices for hypoglycemia unawareness:

- Check blood sugar frequently specially around bedtime and during exercise
- **Loosening-up tight glycemic control a little bit**
- Let your family and work colleagues knows about your condition
- Carry glucagon pen and teach your family how to use it if you become unconscious
- If the cause is autonomic neuropathy get small frequent meal and prokinetics drugs
- If drugs fail, then for gastric pacing

MRCP-PACES
Brief Clinical Consultation
Hypopituitarism

You are a doctor in the clinic today
Mrs. Mary is 41 years old complaining of fatigue for 3 months
I did laboratory test which showed sodium of 146, potassium 3.7, hemoglobin 10.9
Please see and advice further
Yours, GP

Confirmations:
- **Self**
- **Patient**
- **Agenda**

Checks:
- Expectations
- Knowledge
- How she feels

Opening question:
- I got a letter from your GP mentioning that you have tiredness for last 3 months; could you tell me more about that?
- Yes doctor, I got this tiredness since last few months and really destroying my life and I took many herbal remedies and vitamins without any help

Empathy and sympathy

Screen briefly for the tiredness:
- How many steps could you manage before getting tired?
- Is it sudden or gradual
- Is it the same since it start – worsening? , improving?
- Anything improves it or worsens it?
- Any associated other symptoms?

Association:
- Any headache
- What about your mood?
- What about your sleep? Are you getting good sleep?
- **Any joint pain?**
- Any exercise?
- Any trauma?
- Any history of fractures or weak bones?

Differential diagnoses:
Hypothyroidism:
- Any weight change?
- Any neck swelling

- Any weather preference

Addison's:

- Any dizziness
- Any skin pigmentation?
- Feeling sick or getting sick?

Chronic fatigue syndrome- fibromyalgia

- Any muscle pains and aches
- Any headache
- Lack of sleep
- Any problem with thinking and concentration

Anemia:

- Any blood loss
- Getting pallor than usual
- Heart racing

Multiple sclerosis:

- Any weakness
- Any sensory loss
- **Any disturbance of your eye sight?**

Malignancy:

- High body temperature
- Pumps and lumps
- Weight loss

Surgical history:

- Any surgery done?

Drug history:

- Medication list
- Allergies

Family history:

Social history:

- What is your job?
- How symptoms affecting you at work and in daily life activity?
- May I ask you a private question?
- Do you have a partner?
- What about your intimate relationship?
- Did you got pregnant or any chance of pregnancy?
- **No doctor, My period is not coming for last 6 month and I did test for pregnancy and was negative**
- Do you smoke?
- Do you drink alcohol

Can I examine you?

- **Pallor**
- **Visual field -** bitemporal hemianopia
- **Fundoscopy**
- Neck – **thyroid**
- **Skin is soft, dry and wrinkled, no hyperpigmentation**
- **Oral cavity and lips –** hyperpigmentation

- Decreased **facial** and **body hair**
- If male offer to examine the **breasts** - gynaecomastia
- If male also offer to examine **testes** - testicular volume
- Comment on **muscle bulk**
- **Blood pressure – postural drop**
- **Check blood sugar**

What is your concern?

What's wrong with me doctor?

- From what you told me and after I examined you , you have a problem in master gland in your brain controlling different glands in your body
- That gland is not functioning well , producing less protein called hormones controlling other body glands like gland in your neck and glands overlying kidneys and your ovaries leading to symptoms you have of tiredness, no menstrual cycles
- There is no clear cause of why the master gland of your brain is not functioning , many possibilities are there
- What we need to do is to do some blood tests and imaging to confirm our diagnosis and to rule out others

Questions commonly asked by examiners

What are your clinical findings?

- **Pallor**
- **Alabaster skin**

What is your clinical diagnosis?

- **Hypopituitarism**

What are the differential diagnoses for the hypogonadism in this case?

1. **Pituitary mass**
    i. Adenoma
    ii. Metastasis
2. **Infiltrative disease**
    i. Sarcoidosis
3. **Pituitary infarction (Sheehan's syndrome)**
4. **Pituitary apoplexy** – against it no history of bleeding
5. **Trauma**

What are the differential diagnoses for the hypogonadism in this case?

1. Primary hypogonadism
2. Pituitary failure with secondary hypogonadism

How you will investigate this case?

- **Basic investigations:**
- CBC, chemistry, inflammatory markers
- TFT
- Serum cortisol
- Gonadotrophins – LH, FSH

- GH level
- Brain MRI/CT scan

What are the causes of pituitary failure?

- **Pituitary mass**
    - Adenoma
    - Craniopharyngioma
    - Cyst
    - Metastasis.
- **Pituitary surgery or radiotherapy**
- **Infiltrative disease**
    - Sarcoidosis
    - Haemochromatosis
    - histiocytosis X
    - Lymphocytic hypophysitis -lymphocytic infiltration of pituitary during late pregnancy/ postpartum.
- **Pituitary infarction (Sheehan's syndrome)**
    - Typically following postpartum haemorrhage and consequent hypovolemia.
- **Pituitary apoplexy**
    - Sudden haemorrhage into the pituitary gland, most commonly into a pituitary adenoma.
- **Empty sella syndrome**
- **Trauma**
- **Subarachnoid haemorrhage**

What do you understand by the term 'empty sella syndrome'?

- This refers to an **enlarged sella turcica**, which is **not entirely filled with pituitary tissue**.
- This may be **secondary to surgery, radiotherapy, or infarction**, and may cause hypopituitarism.
- However **primary empty sella syndrome** is **not associated with hypopituitarism**, since the sella is enlarged by cerebrospinal-fluid (CSF) pressure through a defect in the sella membrane, and there is no deficit of pituitary tissue.

What are the clinical presentations of hypopituitarism?

- The presentation depends on the onset of the condition, which pituitary hormones are deficient, and whether there are local symptoms such as headache or visual loss.
- As a general rule, in progressive pituitary disease, the **secretion of GH and gonadotropins is affected before ACTH and TSH**.
- Sudden insults to the pituitary gland, such as infarction or apoplexy, may cause rapid life threatening ACTH deficiency and hypotension.
- **Slowly progressive disease**, due to radiotherapy or infiltrative conditions, **may present initially with hypogonadism**.
- GH deficiency-in children, GH deficiency causes short stature.
- In adults, this causes decreased bone density and muscle mass; and possible diminished sense of well-being.
- GH replacement is licensed in adults with severe deficiency.
- **Gonadotropin deficiency**

        - In males, this causes testicular hypofunction, erectile dysfunction, and infertility.
        - Testicular atrophy and gynaecomastia are usually clinically detectable.
        - In adults, this may present with decreased libido, decreased facial hair affecting shaving, and eventually loss of body hair and muscle mass.
        - In adult females, this causes similar symptoms to menopausal ovarian failure, such as infertility, amenorrhoea, and hot flushes but there are few consistent clinical signs.
- **TSH deficiency**
    - This causes similar symptoms and signs to primary hypothyroidism.
    - However signs such as weight gain and myxoedema may be obscured by the signs of concomitant ACTH deficiency (weight loss, pallor).
- **ACTH deficiency**
    - This is similar to primary adrenal failure, apart from the lack of pigmentation, and the preservation of mineralocorticoid activity by the renin-angiotensin system.
- **Prolactin deficiency**
- The only manifestation of prolactin deficiency is the inability to lactate following delivery.
- However prolactin may be elevated if there is pituitary stalk compression and viable pituitary tissue

What is the medical management of patients undergoing pituitary surgery?

- All patients undergoing pituitary surgery should undergo pituitary function and visual field testing pre-operatively.
- Check baseline: Free T4,TSH, ·prolactin, oestradiol (females), testosterone (males), FSH, LH, morning cortisol.
- Commence high dose steroid replacement on the day of surgery, with IV hydrocortisone.
- Convert to oral steroid replacement after 72 hours, if there are no post-operative complications.
- Monitor fluid balance and urine osmolality post-operatively, looking for diabetes insipidus (Dl).
- This causes high serum osmolality and low urine osmolality.
- Dl may be transient, but if persists is treated with desmopressin acetate (synthetic analogue of vasopressin) (DDAVP),
- Discharge all patients on oral hydrocortisone, and provide a steroid card and 'medic-alert' bracelet.
- After 3-4 weeks, perform a pituitary stimulation test (insulin tolerance test, metyrapone test, or short synacthen test [preferred test]), following the cessation of steroids the night before.
- Both metyrapone and insulin-induced hypoglycaemia should stimulate ACTH secretion, and therefore test pituitary ACTH reserve.

- In the short synacthen test, although directly stimulating the adrenal tissues, a normal result in this clinical context will only result if the adrenals have been stimulated by sufficient endogenous ACTH from the patient's pituitary gland. If patients fail this test, they require long-term steroid replacement.
- However, some patients recover pituitary ACTH function, therefore patients on steroid replacement should have a further test in two years.
- Measure free T4 post-operatively (the TSH may be normal post-operatively), and replace if deficient.
- Aim to increase the free **T4** within the upper half of normal limit (TSH levels are not a useful guide to the adequacy of replacement)
- If sex hormones are low, then replacement with testosterone or oestrogens in men and women respectively

Clinical notes

- The skin in panhypopituitarism is described as **alabaster skin**, since it is **pale** and **dry**, with an inability to tan due to MSH and ACTH deficiency.
- In males, pituitary gonadotropin deficiency causes testicular hypofunction and loss of secondary sexual characteristics i.e. loss of facial, axillary and pubic hair
- Gynaecomastia is more common in primary hypogonadism, due to a compensatory rise in pituitary luteinizing hormone (LH).
- However secondary hypogonadism due to pituitary failure may be associated with gynaecomastia if treated with gonadotropin replacement.
- Remember to **palpate for breast tissue**, and to differentiate adipose tissue from gynaecomastia.
- Primary hypogonadism is more common than Hypopituitarism, and hence is the most likely diagnosis with these signs.
- Look carefully for signs of congenital conditions causing primary hypogonadism such as Klinefelter's syndrome
- In adults, testicular size should be 4-7cm in length, or 20-25ml volume.
- You will not be expected to perform this test in the examination, but you should assess secondary sexual characteristics such as facial hair, body hair, and body musculature.
- Unlike primary adrenal failure, ACTH deficiency does not cause salt wasting, hypovolaemia, hyponatraemia, or hyperkalemia, since there is no deficiency in mineralocorticoid which is controlled by the renin-angiotensin system.
- However, glucocortioids are required to maintain vascular tone; therefore hypotension may still occur in Hypopituitarism.
- The neurological manifestations of hypopituitarism are due to local effects of the pituitary disease.
- Headaches and **visual field defects** may occur **if the lesion extends** to the **suprasellar region.**
- Lateral extension to the cavernous sinus may affect oculomotor nerves and superior extension may damage the hypothalamus or cause hydrocephalus by occluding the Foramen of Munro.

MRCP-PACES

Brief clinical consultation

Idiopathic intracranial hypertension - IIH

Scenario

You are a **doctor in dermatology clinic**
Mrs. Lara is a 45 years old lady with frequent **headache**

Confirmations:

- Self
- Patient
- Agenda

Opening question:

- You got troubled with headache could you tell me more about that?

Sympathy and empathy:

Analysis of the complaint - headache

ODPARA

- **Onset**
  - Sudden
  - Gradual
- **Course:**
  - Static, progressive, or same
- **Intensity**
  - **Grade 0-10**
- Any other **associated** symptoms like:
  - Change in vision?
  - **If visual obscuration:**
    - **What do you mean exactly?**
      - Seeing double
    - **What do you mean exactly by double vision**
      - Seeing two images for one object
  - **Any weight increments?**

    - Where did you put on weight exactly, which part of your body?
    - Intentional?

Screen differential diagnosis:

1. Migraine – aura
2. Tension headache
3. SOL – increase ICP symptoms
    - **Increase by coughing, sneezing, lying down and bending forward**
    - Nausea and vomiting

Past medical history:

- **Do you have any medical condition I should be aware of**
    - HTN
    - Acromegaly
    - Hypothyroidism
    - Cushing's
    - SLE, Sarcoidosis

Family history:

Drug history:

- Show me your **medication list**
- Double D:
    - Dose
    - Duration
- **Medicines:**
    - Isotretinoin
    - Steroids
    - Tetracycline
    - OCP
    - Thyroxine
    - Nitrofurantoin
    - Lithium
- Vitamin A

Social history:

- QOL- How much symptoms are affecting you?
- Job

- Smoking
- **Driving:**
  - **Stop**
  - **Inform DVLA**

Physical examination:

- General look, obese
- **? Round face, acne**
- Visual acuity- usually intact
- Visual fields- peripheral visual field constriction, tunnel vision due to papilledema
- Eye movements:
  - **6th nerve palsy, lateral gaze palsy**
- **Fundoscopy**-bilateral papilledema
  - If chronic may lead to **optic atrophy** and **blindness**

Addressing concerns:

What is wrong with me doctor?

- From what you told me and after examining you, most likely you have condition called IIH,
- It is a medical term for a medical condition in which there is increase pressure inside your head
- The brain and the main nerve cable in your back are bathed by a clear watery fluid called CSF within the skull.
  in IIH there is raised pressure within the skull which puts pressure on the brain and this will give pressure to back of the eye where the nerve cable responsible for vision called optic nerve is situated.
- It gets swollen and if not treated, might lead to blindness.
- We need to do some blood tests and imaging to confirm our diagnosis and to rule out others
- We will give you medications to relieve your headache and will ask eye doctor to see you and will refer to brain doctor.

Is it due to cancer?

- We need to rule out all causes increasing pressure inside your head, cancer can cause that we need to rule it out

Examiners' questions:

What is your finding

- Obese lady with papilledema and 6th nerve palsy

What is your diagnosis?

- Idiopathic intracranial hypertension

What you will do for this patient?

- **Basic investigations:**
  - CBC, Chemistry, inflammatory markers
  - Coagulation profile
- **Imaging:**
  - MRI/CT Brain:
    - To rule out intracranial lesion
    - LP, to measure opening pressure - after above scans
  - **Bed side US:**
    - Measures diameter of optic nerve sheath
- **Detailed ophthalmic assessment:**
  - Formal **perimetry**
  - OCT

Treatment:

- **General:**
  - Treat obesity
  - Weight loss
  - Diet
  - Exercise
- **Drugs:**
  - Discontinuation of steroids
  - **carbonic anhydrase inhibitors - Acetazolamide**
  - **NSAIDs** and **paracetamol** for headache
  - **diuretics**
- **Serial lumbar punctures:**
- **Surgery:**
  - **lumbo-peritoneal shunt**
  - sub-temporal decompression.
  - **Optic nerve sheath fenestration**

- VP shunt

What are the features of benign intracranial hypertension?

- **Dandy's diagnostic criteria:**
  - Patient is **alert**
  - Clinical features of increased intracranial pressure
  - **No localizing** neurological **signs** (except sixth cranial nerve palsy)
  - **Opening pressure** of CSF during lumbar puncture is **>20 cmH2O**
  - **CSF** is of **normal** composition
  - **Normal ventricles** and normal study on **CT or MRI.**

MRCP-PACES

Brief clinical consultation

Idiopathic thrombocytopenic purpura

You are on-call in the **MAU**.
Mrs. Lara s 45-year-old woman with a history of **easy bruising** who was found to have a **platelet count of 15** × 109/L (150–450 × 109/L

Confirmations:

- **Self**
- **Patient**
- **Agenda**

Opening question:

- You got troubled with **easy bruising**
- Could you tell me more about that?
    - I have been feeling body aching, and a bit of a fever, and
    - I noticed that I was bruising easily over the past week, at the slightest knock or bang.
    - The **GP checked my blood count** and called you because the **platelet level was low.**

Empathy and sympathy:

Analysis of easy bruising – purpura:

- **Where** is the bruising exactly?
    - In your arms or all over your body?
- What is the color?
- Is it painful?
- Is it oozing?
- Is it painful?
- Is it blanchable?
- Since it started is it the same, worsening or improving?
- Any thing increasing it like trauma?
- Anything improving it

Associated symptoms?

- **Any joint pain?**
- Blurring of vision
- Headache?
- Heart racing?
- Loss of appetite
- Weight loss

Bleeding tendency:

- Coughing up blood
- Blood in urine or back-passages
- Any nasal bleed?

Differential diagnosis:

- **Malignancy:**
  - Pumps and lumps
  - Weight loss
  - High body temperature
  - Sweating
- **Aplastic anemia:**
  - Bony aches
  - Getting pallor than usual
- **SLE:**
  - Skin rash related to sun exposure
  - Mouth soreness
  - Joint pain
- **Antiphospholipid syndrome** – history of blood clot
- **Liver disease:**
  - Tummy pain
  - Getting yellow discoloration of white part of eyes
- **Viral infection:**
  - Flu symptoms
- **TTP**
  - Change in water work
- **HUS**:
  - Lose motion
- **Hypersplenism:**
  - Dragging pain in left upper tummy

Endurance

- **HIT** – recent blood thinning medication
- **DIC** – recent bug infection

Past medical history:

- Any past medical history of note?
- Any history **of bleeding disorder**
- Any history of **low platelets** in the past
- Any **blood transfusion** before?
- Hospitalization

Family history:

- History of bleeding disorder in the family

Drug history:

- I was taking a small aspirin tablet daily after I read about it reducing the risk of developing bowel cancer.
- Any new medications
- Any blood thinning medications
- Any **herbal** or **alternative medicine** use

Social history:

- Job
- QOL
- Smoking
- Alcohol
- **May I ask you a private question?**
  - **What about your period**
  - I had a period last week and was much heavier than normal and I could not work out why.
  - Any partner?
  - Any history of **loss of pregnancy** – APS

Can I examine you?

- Inspect for bruising
- **Look for petechial rash and ecchymoses**
  - There are multiple purpuric spots on different parts of the body of varying sizes, which are painless, do not blanch on pressure
- Pallor and jaundice

- **Lips and oral cavity**—There are some bleeding spots over the palate
- **Fundoscopy**
  - For fundal hemorrhages
- Face – butterfly rash
- **Lymphadenopathy**
- No sternal tenderness
- Look for signs of **HHT**:
  - **Telangiectasia** (face, lips, tongue [and underneath], buccal and nasal mucosa, palate and on fingers); can also be cyanosed and clubbed
- **Abdominal**: splenomegaly

What is your concern?

Why are my platelets low?

- After what you told me and after examining you, it is likely that you have a condition affecting the level of platelets, called idiopathic thrombocytopenic purpura (ITP).
- Your platelets are low because your body defense system is destroying your own platelets.
- The platelets are cells in the blood which help the blood clot, and low levels of platelets would explain the bruising you have been having.
- It may well be due to a viral infection
- We need to send some blood tests and imaging
- We need to find out why it has happened, as well as giving you some treatment to increase the level of platelets in the blood.
- I will refer you to the blood doctors
- I advise you to avoid risky situations like fall and trauma and do not blow your nostrils forcefully on cleaning

Am I going to get bowel cancer like my dad did?

- Your father developing bowel cancer at age 72 means that you are at the same risk of developing colorectal cancer as the rest of the population – your father's history doesn't put you at an increased risk of developing colorectal cancer.
- You do not need any investigations/examinations, e.g. colonoscopy, for this.

- If you had a first-degree relative under 50, or two first degree relatives, who had colorectal cancer then under British Society of Gastroenterology guidelines, screening colonoscopy would be indicated +/− clinical genetics input

What is the most likely diagnosis?

- Idiopathic thrombocytopenic purpura (ITP) is the most likely diagnosis

Why?

- Because there are multiple purpuric spots, no history of taking any drugs or secondary causes.

What are your differential diagnoses?

1. **Idiopathic thrombocytopenic purpura**
2. **Acute leukemia**
3. **Aplastic anemia**

Why not acute leukemia?

- It may be acute leukemia, but less likely because there is no fever, lymphadenopathy, hepatosplenomegaly, and bony tenderness.

Why not aplastic anemia?

- There is no history of any secondary cause like drugs, radiation, etc.
- Usually there is severe anemia, bleeding is usually in the form of ecchymoses or bruises.
- But it should be excluded.

What investigations do you suggest in ITP?

- **FBC**
  - Hemoglobin, platelets count
- **LFTs**
- RFT – creatinine and urea
- **DIC investigations:**
  - PT, APTT
  - Bleeding time is prolonged, but clotting time is normal in ITP
  - fibrinogen
- **Blood film:**
  - Red cell fragments in microangiopathic hemolytic anemias - TTP, HUS
- **Autoimmune serology:** ANA positive in 44%

    - **HIV serology:** NB need to explain to patient why this is being sent, obtain consent, and plan for the result to be communicated back to the patient
    - Viral hepatitis serology
- **Bone marrow**
    - increased immature megakaryocytes - may be normal sometimes)
- **Antiplatelet antibody** is present in 60 to 70% cases
- **Anticardiolipin antibody** is positive in 30% cases.

What are the causes of thrombocytopenia?

1. Less production:

- **Aplastic anemia**
- **Bone marrow infiltration**
    - Secondary deposit
    - Multiple myeloma
    - Leukemia
    - Lymphoma
- **Marrow suppression** by radiotherapy or cytotoxic drugs
- **Megaloblastic anemia –** B12 and folate deficiency
- **Myelofibrosis**
- **HIV**

2. Excessive destruction or consumption:

- **Immune**
    - **ITP**
    - drug induced - heparin, thiazide, penicillin, quinine
    - SLE
    - CLL
    - Virus
    - posttransfusion.
- **Nonimmune**
    - DIC
    - TTP
    - HUS
    - Hypersplenism
    - Massive blood transfusion (dilutional).

What is idiopathic thrombocytopenic purpura?

- It is a type of thrombocytopenic purpura due to autoantibody against platelet **(IgG type).**
- The auto-antibody forms against platelet membrane **glycoprotein IIb and IIIa**, which causes premature removal of platelet by monocyte macrophage system.

What are the presentations of ITP?

- In adult—**common in female**, usually insidious onset without preceding viral infection.
- Presents with purpura, easy bruising, epistaxis, or menorrhagia.
- Features of SLE may be present at presentation or may develop after long time.
- It may be associated with other autoimmune diseases like thyroid disorder and autoimmune hemolytic anemia, chronic lymphocytic leukemia, solid tumor, HIV infection.
- On physical examination—apart from bleeding points, no other physical findings.
- **Splenomegaly** is rare (in 10%).

Note Remember the following points:

- Spontaneous bleeding occurs when the platelet is < 20,000/cmm
- At higher count, there may be bruising, epistaxis and menorrhagia
- If platelet count is > 50,000/cmm, there may not be any features, diagnosed on routine test.

What are the diseases to be excluded if ITP is suspected?

- Commonly SLE is to be excluded.
- In 10% cases, thrombocytopenia may be the initial manifestation of SLE for many years.
- Primary antiphospholipid syndrome may present with thrombocytopenia.
- Other primary hemorrhagic disorders should be excluded.
- For this purpose, following investigations should be done
    - ANA, anti-ds-DNA, antiphospholipid antibody and anticardiolipin antibody

- Bone marrow

Note Remember these points:

- In 10% case, ITP may be associated with autoimmune hemolytic anemia called **Evan's syndrome**.
- **Patient > 65 years** old should have bone marrow examination to look for accompanying **B-cell malignancy.**
- **HIV testing** should be considered if there is strong suspicion.

How to treat ITP?

- Most patients with platelet count > 30 × 109/L are stable and do not require treatment unless they are about to undergo a surgery.
- **Management of acute ITP** (symptomatic thrombocytopenia when platelets <10):
  - **First line therapy:**
    - **Prednisolone**
      - 1mg/kg, to be given for 4 to 6 weeks, then tapered.
      - 66% will respond, but relapse is common when the steroid dose is reduced or stopped.
      - 10 to 20% usually have long term remission.
      - If relapse, steroid should be started again.
    - **IV immunoglobulin**
      - may be given, mainly if there is severe hemostatic failure or slow response to steroid alone or surgery is required.
      - Dose of immunoglobulin is 1gm/kg for 3 to 5 days.
      - Its effect is temporary, persists for 3 to 4 weeks and it is quite expensive.
      - Steroid may be added with immunoglobulin.
  - **Second line therapy:**
    - If there is frequent relapse (usually 2 relapses), in primary refractory disease or require high dose of steroid to maintain safe platelet level, **splenectomy** should be done.
    - There is complete remission in 70% cases and improvement in 20 to 25% cases.
    - 5 to 10% require further medical therapy.

- **Third line therapy:**
  - If there is **failure after splenectomy**, other therapy should be considered
    - **anti-D infusion**
    - **danazol**
    - **immunosuppressive therapy**
      - **azathioprine**
      - cyclophosphamide
      - **dapsone**
      - vincristine
      - **vinblastine**
      - ciclosporin
      - mycophenolate mofetil
  - **Monoclonal antibody - rituximab**
  - **Thrombopoietin receptor agonists**
    - Stimulate platelet production in the bone marrow
    - Increased risk of blood clots
      - **ROMIPLASTIM**
      - **ELTROMBOBAG**
- **Platelet transfusion**
  - is not usually used.
  - However, it is used only if persistent or potentially life-threatening bleeding or where emergency splenectomy is done
- Note Remember the following points
  - In no responder after splenectomy, think of presence of **accessory spleen** (confirm by **radionuclide scan**).
  - After splenectomy, there is more chance of infection by Pneumococcus, Meningococcus and H. influnzae (vaccination against these is essential).

EXTRA NOTES:

Q. What are the **differences** between ITP in children and adults (or acute and chronic ITP)?
A. As follows:

Features	Child (acute)	Adult (chronic)
1. Age	Usually 2 to 6 years	20 to 30 years
2. Sex	Any	Common in female
3. Onset	Acute	Chronic
4. Previous infection	Common	Unusual
5. Platelet count	<20,000/cmm	>20,000/cmm
6. Spontaneous remission	Common	Less <20%
7. Duration	2 to 4 weeks	Chronic, months to years

What is purpura? What are the types?

- It is the **spontaneous bleeding or extravasation** of blood from the capillary in the skin and mucous membrane that does not blanch on pressure, and there is progressive color change.
- There are **two types of purpura**:
    - Small and discrete of pin head size, called **petechiae**.
    - Large and ill defined, called **ecchymosis**.

What are the causes of purpura?

- Thrombocytopenic
- Vascular
- Coagulation defect.
- Thrombocytopenic purpura:
    1. Primary or ITP.
    2. Secondary:
- Aplastic anemia (due to any cause)
- Leukemia
- Secondary deposit in bone marrow
- SLE
- Others—DIC, CLD and TTP (thrombotic thrombocytopenic purpura), massive blood transfusion.

Vascular purpura:

- **Congenital** (hereditary hemorrhagic telangiectasia, Ehlers–Danlos syndrome).

- **Acquired**:
    - Senility (in elderly)
    - Henoch-Schönlein purpura (in children, and rarely in elderly)
    - Drug-induced (NSAIDs, thiazide, steroid, sulfonamide, penicillin and thiouracil)
    - Infections—SBE, typhoid, meningococcal infection, septicemia, and viral infections (infectious mononucleosis, measles, chicken pox, dengue hemorrhagic fever)
    - Scurvy
    - Metabolic disorder (CRF and Cushing's syndrome)
    - Collagen disease (RA and SLE)
    - Paraproteinemia (purpura is due to vasculitis or thrombocytopenia or platelet functional abnormality)
    - Amyloidosis (periorbital).

Coagulation abnormality:

- Hemophilia.
- Christmas disease.
- Anticoagulant therapy.

What are the common causes of purpura according to the age?

- In the elderly, the causes are:
    - Senile purpura (usually on extensor surface of forearm and leg).
    - Drug induced purpura (distribution is like senile purpura), and the usual drugs are steroids, NSAIDs and anticoagulant.
    - Leukemia.
    - Aplastic anemia.
    - Scurvy.
    - Paraproteinemia.
- In young or child, the causes are:
    - ITP
    - Henoch-Schönlein purpura (involving buttock and legs)
    - Drug induced
    - Acute leukemia

    - Infections—viral (dengue) or meningococcal septicemia.
- Note In any age, mention the causes as follows (if present):
    - If Cushingoid facies, due to steroid
    - If patient looks toxic, due to septicemia
    - If evidence of RA, SLE, due to disease itself or due to NSAIDs or steroids.

In a child, there is purpura in the leg. What else do you want to see?

- Purpura in buttock, history of arthritis, abdominal pain, bloody diarrhea, hematuria (all features are suggestive of Henoch-Schönlein purpura).

What should you examine in a patient with purpura?

- Whether they blanch on pressure or not (purpura does not blanch).
- Whether they are palpable and painful or not (palpable painful purpura is of vascular origin and nonpalpable purpura indicates thrombocytopenia).
- Color change (progressive color change in purpura from red to dark pigmented).
- Distribution of purpura:
    - Buttock, ankle (Henoch-Schönlein purpura).
    - Extensor surface of forearm, dorsum of hand, leg (senile purpura and drugs).
    - Generalized purpura.

What are the differential diagnoses of purpura?

- **Drug rash**
- **Spider angioma or telangiectasia** (blanch on pressure, but purpura does not)
- **Erythema nodosum** (painful and nodular)
- **Mosquito bite** (usually blanch on pressure, but sometimes may not blanch, if there is extravasation of blood)
- **Campbell de Morgan spots** (common in elderly)—these are small, nodular, reddish lesions that do not blanch on pressure, occur on trunk and upper abdomen, and resolve spontaneously.
- These are benign angioma, common in middle aged and elderly.

- Malignant change occurs rarely (suggested by itching, rapid increase in size and increased pigmentation).

What investigations should be done in purpura?

- Hb%, TC, DC, ESR, platelet and PBF.
- If pancytopenia or thrombocytopenia, perform bone marrow study (dry tap in aplastic anemia, increased megakaryocyte in ITP).
- Other investigations (according to suspicion of causes):
    - Coagulation screen (BT, CT, PT, APTT and FDP) for hemophilia and Christmas disease and other coagulation factors, screening for DIC.
    - Blood culture (if septicemia).
    - ANA, anti-double-strand DNA (for SLE).
    - Anti-phospholipid antibody.
    - Liver function tests (in CLD).
    - Renal function tests (in CRF).

What is Hess's test?

- It is a bedside test, also called tourniquet test.
- In this test, a sphygmomanometer cuff over the upper arm is inflated in between systolic and diastolic pressure, wait for 5 minutes.
- Then deflate the cuff, wait for another 5 minutes.
- Look for petechiae in cubital fossa and near the wrist.
- Normally, there may be <5.
- If >10, it is an indication of thrombocytopenia.
- If >20, then abnormal.
- If platelet is <60,000, it is usually positive.
- Causes: Thrombocytopenia or platelet functional abnormality or increase in capillary fragility (This test is frequently done to diagnose dengue hemorrhagic fever).

What are the causes of platelet functional abnormality?

- Platelet functional abnormality (thrombasthenia) occur in:
    - Chronic renal failure
    - Chronic liver disease
    - Paraproteinemia

- Myeloproliferative diseases
- Drugs—NSAIDs (aspirin, indomethacin, and ibuprofen).

How does TTP present?

- Clinical presentation classically reported as five components: microangiopathic hemolytic anemia (MAHA), thrombocytopenia / purpura, neurological impairment, renal impairment, fever (e.g. young woman with fluctuating neurological signs, fever, renal impairment and microangiopathic hemolytic anemia).

Q. How to **differentiate** in bleeding or purpura whether due to bleeding abnormality or coagulation abnormality?

A. As follows:

Coagulation abnormality	Bleeding abnormality
1. Family history usually present	Family history may or may not be present
2. There is history of prolonged bleeding	No history of prolonged bleeding
3. Usually there is bleeding into the joint or muscle, purpura is less common or rare	Bleeding into the skin and mucous membrane, purpura is more common
4. Clotting time is prolonged, but bleeding time and platelet count are normal	Clotting time is normal, but bleeding time is prolonged and platelet count is low
5. Particular coagulation factor is low or absent, e.g. in hemophilia, factor VIII is absent or low	Coagulation factor is normal, and it is due to either low or defect in platelet function or vascular defect

What is Felty's syndrome?

- Rheumatoid arthritis with splenomegaly and neutropenia is called Felty's syndrome.
- There may be hypersplenism (anemia, leukopenia, and thrombocytopenia).
- It occurs in long standing, seropositive, deforming, but inactive arthritis, in < 1% of the cases.
- Female is more affected than male, age 50 to 70 years.
- Leg ulcers or sepsis are complications due to neutropenia. Splenectomy may be necessary for hypersplenism.
- It is associated with high titer of rheumatoid factor, subcutaneous nodules, and other manifestations of systemic rheumatoid disease.

MRCP-PACES

Brief clinical consultation

NAFLD

Your role: you are an **ST2 in the diabetes clinic**
Jeremy Somers, a 65-year-old man. has come to see you.
His GP has forwarded to you some recent blood results which show an **elevated ALT of 92** (usual <41), **γ-GT 102** (usual <50).
The GP reports that the patient has **diabetes** with **good control**, with **slightly raised cholesterol** and a BMI of 32, and the GP is asking for your help in investigating why the liver tests are elevated.
The patient's **recent HbA1c was only very slightly above normal**.
ALT was 60 2 years ago with otherwise **normal LFT**.
Ferritin 500.
Your task: to assess the patient's problems and address any questions or concerns raised by him.

Confirmations:

- Self
- Patient
- Agenda

Opening question

- **I receive a letter from your GP mentioning raised liver function blood test done for you, could you tell me more about that?**
    - I went to my GP to have some **routine blood tests** for monitoring as I am on a '**statin' tablet for my cholesterol**.
    - He had mentioned to me that I have slightly raised liver tests last year but said that it was probably due to my diabetes.
    - A new locum GP was there because my usual GP was on holiday, and he called me back in and told me that my liver was not working as well as it should, and I may need a snip of my liver.

- He explained that the diabetes specialists were due to see me and they could decide.

Empathy and sympathy:

Screen for symptoms associating increase LFTs:

- **Any tummy pains**
- **Yellow discolored** of the white part of eyes
- Getting **pallor** than usual
- **Weight change**
  - Increased
  - nonintentional
  - 10 kilos in last 6 months
  - fatty food
- Any chest pains

Screen for differential diagnoses of increased LFTs:

1. **Viral hepatitis and HIV:**
   - No transfusion
   - No tattooing
   - No piercing
   - No illicit drugs
   - No recent travel
2. **Malignancy:**
   - No high temperature
   - No pumps or lumps
3. **NASH-NAFLD:**
   - Are you diabetic?
   - For how many years
   - What do you take?
   - Is it controlled?
   - What is the last 3-month sugar reading
   - Diet
   - Exercise
   - Vision problem
   - Water work, etc.
   - Any HTN?
   - Any high Cholesterol?

- **D- Hemochromatosis:**

- Hyperpigmentation
- Joint pain
- Problem with intimate relationship

Past Medical History:

- Did you get yellow - jaundice
- PH of liver disease
- Surgeries

Drug History:

- Allergies
- Metformin 1 g bid
- Gliclazide 80mg bd
- Atorvastatin 40mg od
- Ramipril 2.5 od
- **Any herbal/alternative medicines?**
- **Any over counter medicines?**

Family History:

- Similar condition
- **Anyone got yellow - jaundiced**
  - My father had problems with alcohol and developed cirrhosis from which he died aged 65
- Family history of haemochromatosis
- **Any one in family ever needed venesections**

Social history:

- What do you do for living?
- Do you have a partner?
- Do you drink alcohol?
- **How many units per week and what strength?**
  - I have 3 pints of lager (4%) every Saturday night, and avoid drinking during the week
  - Never had a problem with drink, and I do not think that I drink excessively
  - I have never been told what the right amount is to drink per day or per week
  - It is never caused me any health problems in the past

Can I examine you?

- Jaundice
- **Xanthelasma**
- **BMI - obese**
- **LNs** - cervical, supraclavicular
- **Skin- Tattoos, piercings, injection sites**
- **Signs of CLD:**
  - Protein calorie malnutrition - muscle wasting
  - Leukonychia, Clubbing
  - Dupuytren's contracture
  - Palmar erythema
  - Hepatic flap
  - Parotid enlargement
  - Gynaecomastia
  - Spider naevi
  - Hepatomegaly - if fatty
  - Ascites, LL edema
- **Signs of haemochromatosis:**
  - Skin pigmentation - bronzed/grey
  - Hepatomegaly ± splenomegaly
  - Signs of CLD
- **NAFLD:**
  - Central obesity
  - No sign of CLD
- **Blood sugar check marking** in pulps of fingers
- Check **urine** for **sugar**
- Check **BP**

What is your concern?

What is wrong with me?

- **After what you told me and after I examined you**, most likely the elevated liver blood tests found by your GP are due to increased amounts of fat in the liver, a **condition called fatty liver**
- This is related to you having DM, raised cholesterol and being overweight. We will send off a collection of blood tests to look for other causes of raised liver blood tests such as infections in the liver, or inflammation, and arrange an US scan to look at the liver.

- I will arrange for you to go and see the liver doctors after these tests have been done.
- The main treatment of fatty liver is through the ongoing treatment of your high blood sugar and cholesterol, as well as weight loss + reduced intake, increased exercise, aiming for gradual sustainable weight loss, and healthy living

Am I going to get liver irreversible damage?

- Although the risk of developing scarring in your liver from having fatty liver is low, it is really a warning shot for the need for healthier eating, more exercise, weight loss etc. to reduce the risk of diabetes-related vascular complications in the long term, e.g. Stroke, heart attacks, etc.

Why is my GP worrying about my liver now after 2 years?

- One of the liver blood tests (ALT) was higher this year compared to the previous time (last year) and your GP wanted a full check-up of the liver, an MOT, to rule out any other causes (unrelated to diabetes/fatty liver) requiring different treatment.

Do I need a liver biopsy?

- We will send off all the tests, arrange the scan and the liver doctors will see you and
  decide on further management.
- They may advise a biopsy if they think that it will provide useful information that blood results do not

How much alcohol can I drink every day?

- The standard advice is **<21U/ week for a man** (maximum of 3–4 units per day with several alcohol-free days per week) but you need to be aware of the **calorie intake** associated with alcohol, and the **risk of weight gain** due to this

Examiners' questions:

What are your findings?

- Looks obese
- Central obesity

What are your differential diagnoses

1) **NAFLD**

Predisposing causes for this include obesity, DM, raised cholesterol
- metabolic syndrome – leads to fat deposition in the liver

2) Haemochromatosis

- Raised ferritin in patient with DM
- Needs HFE genotype test to look for genotype
- Raised ferritin can also be due to increased alcohol intake or inflammation, e.g. other acute phase reaction e.g. Viral hepatitis can lead to an elevated ferritin

3) Viral hepatitis

How you will investigate this case?

- **Basics investigations**
  - ESR, CRP
  - LFTs
  - Synthetic function - INR, albumin, platelets
- **Full liver screen:**
  - Hepatitis B surface antigen
  - Hepatitis C antibody
  - **Immunoglobulins**
  - Antimitochondrial antibody
  - Anti-smooth muscle antibody
  - **Anti-liver kidney microsomal antibody**
  - ANA
  - Ferritin
  - **α1-antitrypsin**
  - α-FP
  - Caeruloplasmin - <40 years
- **Ultrasound to exclude**
  - Focal lesion(s)
  - Biliary obstruction
  - Echogenic livers consistent with fatty change
  - US has poor sensitivity/specificity for cirrhosis

- **How you are you going to manage this case?**
  - **Non- pharmacological:**
    - **Education and counseling**
    - **Alcohol:**
      - Advise patient to stick to recommended limits in DM.
      - **Increased risk of hypoglycemia** with alcohol- **180 calories in each pint** of standard strength 4% **lager** as weight loss is a core part of the management of fatty liver
    - **NAFLD:**
      - Weight loss
      - Management of the metabolic syndrome
    - **MDT:**
      - Referral to gastroenterology to investigate the elevated LFT.
      - They will decide on the likelihood of him having NAFLD, NASH or cirrhosis, and whether he needs a liver biopsy based on the results of the full liver screen and imaging
    - Noninvasive methods for guiding the decision on whether a biopsy is required include **scoring systems** such as the **BARD** or **Angulo scores**, and newer, non-invasive assessments of the degree of liver fibrosis such as '**fibro-scans'** are available in some centers; these methods all aim to **assess the degree of fibrosis in the liver** without the need for a biopsy.
    - **Liver biopsies**
      - May then be carried out in patients with scores suggestive of fibrosis or cirrhosis, as this can guide further management

What are the features of the metabolic syndrome?

- Various definitions exist.
- The International Diabetes Federation criteria in 2006 require:

1) **Central obesity**

- **Waist circumference**- combined with **two of:**

1. **Hyperlipidaemia:**
    a. **Elevated triglycerides** or on **treatment** for this
    b. **Low HDL** or on **treatment** for **elevated HDL**
2. **Hypertension or on treatment**
3. **DM**
    - **Elevated fasting plasma glucose (>5.6mmol** – preferably confirm with oral glucose tolerance test) or previously diagnosed type 2 diabetes

MRCP-PACES

Brief clinical consultation

Nelson Syndrome

Scenarios:

- Skin hyperpigmentation
- Diminution of vision
- Loss of vision
- **Hypopituitarism -** Frequently, only partial hormone deficiencies occur

You are SHO in the clinic
23 years old Miss. Lara, complaining of **headache**

Background and opening question:

- You have been troubled with headache
- Could you tell me more about that?
    - Yes doctor, since last 1 year I have this headache and it is really destroying my life

Brief analysis of complaint:

Headache:

ODPARA

- Which part of your head
- Nature
- What grade of pain 0-10
- Increase by coughing, sneezing, and bending forward
- Anything increasing it
- Anything decreasing it

Screen for symptoms of ICP:

- **Blurring of vision:**
    - What do you mean exactly by blurring of vision:
        - **Not seeing side of road**
    - Bumping to objects

endurance

- When did it start?
- Sudden or gradual?
- Is the night vision affected?

    - **I am also frustrated with reading because it is difficult for me to pick up the beginning of the next line.**

- Feeling or getting sick?
- Difficulty moving the eyes
- Double vision
- Numbness on the face
- Any weakness anywhere?
- Any alteration of sensation?

Screen of other hormone alteration due to pressure symptoms and hypopituitarism:

- **Reduced TSH - Hypothyroidism:**
    - Weight change
    - Low mood
    - etc.
- **GH deficiency:**
    - Reduced exercise capacity
    - Excessive tiredness
- **Deficiency of gonadotrophic hormones - LH and FSH:**
    - Loss of menses
    - Problems with intimate relationship
- **Increase MSH:**
    - Any skin hyperpigmentation?
    - Pigmented scars
    - Pigmented lips or gum

Screen MEN1: ☆

1. **Pituitary adenoma**
2. **Pancreatic** - insulinoma - symptoms when feel hungry
3. **PTH adenoma**: Acid burn sensation, Passing stones

Past Medical History:

- Medical condition I should be aware of
- **Any surgery:**

endurance

- Head
- Abdomen

Family history:

Social history:

- **QOL-** how much these symptoms affecting you in daily activity and at work**?**
- Job
- Smoking
- Alcohol
- **May I ask you private questions if you allow me?**
- **Do you have a partner**
- **Any problem with the intimate relationship?**
- **What about your period?**
- Driving?
- **I strongly advise you to stop driving and to inform the DVLA**

Can I examine you?

- General look - **tanned patient**
- Visual acuity normal
- Visual field when you see my finger tell me - restricted = **Bitemporal hemianopia**
- **Fundoscopy:**
    - **Optic Atrophy**
    - **Papilledema**
- **General examination:**
    - Pulse
    - Pallor
    - Jaundice
    - Mouth - hyperpigmentation
- **Abdomen:**
    - Scars of surgery - move index finger on them, adrenal and trans-sphenoidal or trans-frontal

What is your concern?

What is wrong with me?

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- From what you told me and after I examined you, most likely you have a condition called Nelson's syndrome
  It is a medical term for a medical condition in which there is:
  Overgrowth of gland in your brain producing increase protein in body due to removal of two glands overlying your kidneys leading to symptoms you have
- What we need now is to arrange some blood test and imaging and special tests to eyes
- Then will sit with you to discuss the plan of management which is most likely will involve treatment by group of specialized doctors including gland doctor, brain surgeon and radiotherapist to give the proper plan of management
- For the time being we will give pain medication for the headache and I advise you to stop driving
- **Is that okay with you?**

Is it going to affect my son?

- Nelson's syndrome only occurs in patients with medical condition called Cushing's disease if they have had both glands overlying both kidneys removed.
- Most cases of Cushing's disease are not inherited, but rarely, these tumors can be part of a disease run in family, called multiple endocrine neoplasia.

Examiners' questions:

What are your findings?

- Bitemporal hemianopia
- Hyperpigmented skin
- Scars of adrenalectomy bilaterally

What is your diagnosis?

- Nelson's Syndrome

What is Nelson syndrome?

- Nelson's syndrome is the term used to describe an enlargement of an adrenocorticotropic hormone-producing tumor in the pituitary gland, following surgical removal of both adrenal glands in a patient with Cushing's disease.

- The tumor produces an excess of a hormone called adrenocorticotropic hormone due to loss of negative feedback from adrenals to pituitary gland

What are your differential diagnoses?

1. Addison Disease
2. Adrenal Hypoplasia
3. Autoimmune endocrine conditions
4. Congenital Adrenal Hyperplasia
5. Craniopharyngioma
6. Ectopic secretion of ACTH
7. Hemochromatosis
8. Neurofibromatosis Type 1
9. Nonfunctioning pituitary adenomas

How you will investigate this case?

- **Basic investigations**
  - Inflammatory markers
- **High ACTH level**
  - Adrenocorticotropin (ACTH) measurement levels are markedly elevated in Nelson syndrome, usually in the thousands of picograms per milliliter.
- **Thyroid function tests**
  - **Central hypothyroidism**, which is not always clinically detectable, may be present.
  - Free thyroxine (T4) levels are commonly just below the lower limit of the reference range, and thyroid-stimulating hormone (TSH) levels may be low, normal, or even mildly elevated.
- **Prolactin measurement**
  - Any lesion that disrupts the pituitary stalk or hypothalamic-pituitary portal system results in mild hyperprolactinemia (< 100 ng/dL) because of loss of dopaminergic inhibition.
  - Patients with prolactin-secreting pituitary adenomas typically have levels that exceed 150-200 ng/dL, with levels being many times greater in patients with macroadenomas.

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- **Growth hormone measurement**
  - Insulin like growth factor–1 (IGF-1) and insulin like growth factor–binding protein-3 (IGF-BP3) measurement is a useful means of screening for growth hormone deficiency
- **Gonadotropin measurement**
  - Measure gonadotropin levels in adolescents in whom pubertal arrest or delay is suggested.
  - Hyperprolactinemia causes hypogonadotropic hypogonadism.
  - If androgenization with testicular enlargement, symptoms of pituitary or visual disturbance, and suppressed gonadotropins are present, human chorionic gonadotropin (HCG) should be measured to exclude a germ cell tumor.
- **Urine osmolality or specific gravity tests**
  - Central diabetes insipidus occurs if the tumor has destroyed the posterior pituitary gland or disrupted the stalk.
  - This is a rare occurrence because vasopressin secretion can occur more proximally if impingement on the neurohypophysis is gradual.
- **MRI of the pituitary gland**
  - A gadolinium-enhanced MRI of the pituitary and parasellar region with 3-mm cuts through the pituitary adequately demonstrates the tumor and provides evidence of **compression** or **invasion of surrounding structures**.
- **Visual field assessment**

How is Nelson's syndrome treated?

- **Surgical removal:**
  - Of the pituitary tumor
  - Surgery remains one of the best hopes of cure for patients with Nelson syndrome and is the treatment of choice for large tumors that are producing acute compression of the optic apparatus and other vital structures.
  - **Transsphenoidal** surgery by an experienced surgeon is optimal because it offers the **lowest risk** of hypothalamic injury.
- **Radiotherapy:**
  - May also be used, especially if surgery is not felt to be safe.

- **Stereotactic radiosurgery**, called **gamma knife surgery** (GKS), has been successfully performed in secretory pituitary tumors (including Nelson syndrome tumors) that are refractory to other surgical interventions
- The most serious long-term problems have included learning and memory difficulties, radiation-induced visual damage, and, most importantly, the risk of secondary tumors
- With the advent of newer means of reducing radiation scatter (eg, linear accelerator [LINAC], gamma radiosurgery), radiotherapy-associated morbidity has significantly decreased and may be helpful in tumors that are not amenable to surgery.

- **Medical treatment:**
  - **Shrinking the tumor**
    1. Somatostatin-analogs:
    2. Cabergoline: Dopamine receptor agonist
    3. **Temozolomide:**
       - Chemotherapy used to treat primary brain tumors
  - **Replacement of deficient hormones:**
    - Hormone deficiencies may resolve after removal of the tumor, but these will be treated if symptoms persist.
    - **This may involve:**

A. Thyroid hormone replacement
B. GH replacement
C. Testosterone or estrogen replacement.
D. Steroids replacement:

- Most patients with Nelson's syndrome will already be taking steroid replacement therapy.

Mention some causes of hyperpigmentation

- Suntan
- Race
- Uraemia
- **Liver diseases**
  - Cirrhosis
  - Primary biliary cirrhosis

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- Ectopic ACTH
- Porphyria cutanea tarda
- Nelson syndrome
- Genetic
- Peutz-Jehger's syndrome
- Xeroderma pigmentosum
- **Metabolic**
    - Haemochromatosis
    - Porphyria
- **Drug**
    - OCP
    - Minocycline
    - Amiodarone
- **Endocrine**
    - Addison's disease
    - Cushing's syndrome
    - Nelson's syndrome
- **Pregnancy**
- **Nutritional**
    - malabsorption
    - Kwashiorkor
    - pellagra
- **Post-inflammatory** - eczema

What are the differential diagnoses of scars in loin area?

1. Retroperitoneal laparoscopic adrenalectomy
2. Nephrostomy tube insertion scar

How is Adrenal Surgery Performed?

- Traditional open surgery
- Minimally invasive:
    1. **Retroperitoneoscopic surgery** (goes through the back)
    2. **Laparoscopic trans-peritoneal**

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MRCP-PACES

Brief Clinical Consultation

Neutropenic sepsis

Your role: you are the ST2 in the MAU.
You have been asked to see Mr. Len Rayburn, a 62-year-old man who has been transferred from the acute oncology unit.
The oncology clinical nurse specialist referred the patient with a neutrophil count of 0.1 and fever of 38.3°C.
Pulse was 120, BP 90/55 in oncology, and he was given some intravenous fluids.
Your task: to assess the patient's problems and address any questions or concerns raised by him.

Confirmations:

- Self
- Patient
- Agenda

Opening question:

- You have been referred by the cancer nurse from their acute care unit with high body temperature and low count of body own defense cells
- **Could you tell me more about that?**
  - I have this high body temperature and sweating for last 2 days and I am feeling unwell, my wife called the nurse, we were asked to come immediately, and they took blood test and result came with low count

Empathy and sympathy:

Brief analysis of the complaints:

Fever

ODPARA

- Onset

- Duration
- Progression
- Association- sweating
- Did you take any antipyretic

Analysis of differential diagnoses:

Systemic review:

- **CNS**
  - Headache
  - Neck rigidity
- **HEENT:**
  - Ear pain
  - Throat pain
  - Mouth soreness
  - Chest
  - Cough
- **CVS:**
  - Heart racing
  - SOB
- **GIT**
  - Sick or feeling sick
  - Loose motion
  - Tummy pain
  - Pain in back passages
  - Loss of appetite
- **Skin:**
  - Rash
  - Soreness
  - Soreness in private area

Past Medical History:

- Any PMH I should be aware of?
- Yes, I have bowel cancer
- I had surgery to the bowel
- Any other chronic illness?
- Any previous admissions?

Drug History:

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- Any allergies?
- Are you receiving any treatment?
- Yes, I am getting some medications, they told me it is chemotherapy
- **Oxaliplatin and Capecitabine**
- When did you received it?
- How many times?
- Do you have any inserted blood channels access device - tunneled line - in neck, chest wall or your limbs, through which you are receiving your chemotherapy?
- **Did you received any medicine following your chemotherapy to boost your body defense system?**
- Are you getting medicine called steroids?

Family History:

- Any cancer?
- **Anyone unwell in family?**

Social history:

- With whom you are living
- What you do for living?
- Smoking
- Alcohol
- Any travel?

Can I examine you?

- **Observation chart**
  - Temperature
  - Pulse
  - BP
- Skin of neck, chest, limbs:
- **Any tunneled line in place?**
- **HEENT:**
  - Mouth ulcer
  - Tonsillitis
  - Ear discharge
  - **Neck stiffness**
- **Chest:**

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- Crackles
- **Abdominal:**
  - ✓ Scar of hemicolectomy
  - ✓ Tenderness
  - ✓ Organomegaly
- **Full skin examination:**
  - rash, cellulitis
  - petechiae
  - blistering
- **Note:**
  - **Avoid rectal examination** in neutropenic patients –increases risk of **bacterial translocation**
- Ask to do **urinalysis**
- **Two minutes warning!**

What is your concern?

What is wrong with me?

- From what you told me and after I examined you, you have a condition called neutropenic sepsis, it a term for severe bug infection caused by chemotherapy that you received.
- What we need to do is to admit you , do some blood tests and imaging, start iv antibiotics , and will give medicine that will increase your blood defensive cells count and you will be seen by group of specialist including cancer doctor, infectious disease doctor and dietician to give you the best plan of care
- Is that okay with you?

Does this mean I cannot have chemo again?

- No, you will get it in exact appointment and schedule dependent on full recovery from low count and no complications
- Has it permanently damaged my immune system?
  No, it has not
- We expect your neutrophil count to recover
  on its own within the next few days.

Will it happen every time I have chemo?

- Oncology team will review how you respond to this episode.
- For next cycle you may need:

    - **Prophylactic antibiotics**
    - **Prophylactic G-CSF**
    - **Dose reduction**
- However, if you get a temperature or symptoms of infection after future cycles of chemotherapy, you should present straight away as it has the potential to
  get worse rapidly.

Will it delay treatment?

- It will only delay treatment if neutrophils have not recovered by the time the next treatment is due.

How do you reduce the risk of chemotherapy-induced neutropenic sepsis in future?

- Oncology doctor will review how you respond to this episode.
- For future cycles of chemotherapy, you may need:
    - Prophylactic antibiotics
    - Prophylactic G-CSF
    - Dose reduction
- Same what I told above
- We need to ensure no active sepsis prior to next chemotherapy cycle.

Examiners' questions

What are your findings?

What is your diagnosis?

- Neutropenic sepsis

What are the differential diagnoses?

1. **Neutropenic sepsis as consequence of chemotherapy**
    - Assume neutropenic sepsis in any febrile patient within three weeks of chemotherapy.
    - Do not delay broad-spectrum antibiotics
    - give antibiotics after cultures and within 1 hour of presentation
    - Cause may not be identified.
    - Consider bacterial, viral, fungal causes
2. **Conventional causes of sepsis in patient immunosuppressed by chemotherapy, e.g. CAP/UTI**

How you will investigate this case?

- FBC (neutrophil count), U&E, LFT, CRP,
- ESR, lactate, glucose
- **Septic screening:**
    - Blood cultures:
        - Aerobic and non-aerobic
        - Peripheral and central if central - Hickman line, PICC or porta cath
    - Urinalysis/MSSU
    - Stool culture for MCS
    - C. difficile testing
    - Throat swab
    - **Galactomannan test** - detection of galactomannan in blood is used to diagnose invasive aspergillosis infections
- CXR: exclude pneumonia

How you will manage this case?

- **Non - pharmacologic:**
    - Education and counseling:
        - Avoid crowds
        - Freshly cooked food
        - Hygienic measures
    - Reversed isolation
- **Pharmacologic:**
    - Empirical antibiotics: follow local neutropenic sepsis protocol
    - Anti-pseudomonal single agent example meropenem, tazocin
    - Vancomycin in some cases:
        - Sepsis
        - Skin infection
        - Mucositis
        - Central port - like porta cath
- Aminoglycoside - amikacin in case of septic shock
- Needs first dose of antibiotics as soon as possible after presentation - less than 1h – the golden hour principle
- Antifungal: if fever by 72 hours
- Anti-pyretic

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- **IV fluid resuscitation:**
  - Aim for systolic BP>100, urine output > 0.5mL/kg/h
- **Growth factors:**
  - G-CSF
  - GM- CSF
  - Peg-filgrastim
- Mouth wash - chlorhexidine
- Nystatin drops in case of thrush

What is the role of G-CSF, when to start, and when to stop?

- Consider if hemodynamically compromised or very prolonged period of neutropenia.

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RCP-PACES

Brief Clinical Consultation

Ocular Prosthesis

You are a doctor in the clinic today
Mr. Edwardu is 45 years old with loss of vision in the right eye

Confirmations:

- Self
- Patient
- Agenda

Checks:

- Expectations
- Knowledge
- How he feels

Opening questions:

- You got troubled with loss of eyesight in right side
- Could you tell me more about that?

Brief analysis of loss of vision:

- What do you mean exactly by loss of vision?
- Cannot see anything even light?
- ODPARA

Associations:

- Any headache?
- Do you feel or getting sick?
- Any weakness anywhere in your body?
- Any trauma to the eye?
- Any high temperature?
- Any pumps or lumps?
- Loss of hearing?

Past medical history:

Drug history:

- Any allergies
- What is your medication list?

Surgical history:

- Do you have any surgery in the past?
- Yes eye surgery, I don't know the details, I had bad car crash and I have no details of what got done

Family History:

- Similar condition

Social history:

- What is your job?
- QOL
- Smoking
- Alcohol
- Driving

Can examine you?

- The right **eyeball** has a **glazed appearance**
- The **light reflex is absent** on the right
- The right **pupillary reflexes** (both direct and consensual) are **absent**
- **Visual acuity** – complete blindness
- **Eye movement** – normal !!

What is your concern?

What is wrong with me?

- From what you told me and after I examined you, most likely you have an artificial eye, what we call it ocular or eye prosthesis that was placed instead of your damaged eye during the car accident you had
- We will refer you the eye doctor for follow up
- You can live normally with that
- Is that okay with you?

What is your finding?

- Absent light reflex
- Absent pupillary reflexes
- Complete blindness in the right eye

What is your diagnosis?

- This patient has an ocular prosthesis on the right eye

Clinical notes

- A glass eye is commonly encountered in the short cases of the MRCP (PACES) examination.
- They may be obvious, especially with older eye implants.
- In the current era, it is common for surgeons to attach t he extra-ocular muscles to the implant.
- This creates proper volume of the orbit and allows natural eye movements.

- In such cases it may become difficult to distinguish a natural eye from an artificial one.
- If the candidate is not prepared to encounter such a case, it can cause considerable confusion in the examination.
- The first clue to an ocular prosthesis may be the glazed appearance of the prosthesis.
- Although they are commonly referred to as 'glass eyes', they are made of medical grade acrylic, hydroxyapatite, polyethylene, and in some cases, cryolite glass.
- The triad of absent light reflex, absent pupillary reflexes, and complete blindness should make the diagnosis of an ocular prosthesis straightforward.
- Although the term 'glass eye' is commonly used, it is best avoided-as not all implants are made of glass!

Questions commonly asked by examiners

What the indications for eye removal?

- Malignancy
  - Melanoma
  - Retinoblastoma
- **Trauma**
- **End stage glaucoma**
- **Painful blind eye**
  - **Glaucoma**
  - Endopthalmitis
  - Uveitis
  - Band keratopathy
- **Congenital cystic eye**

MRCP-PACES

Brief Clinical Consultations

Osteomalacia and Rickets

You are a doctor in the clinic
Miss. Lina is 32 years old, has **problem in walking**.
Please assess him

Confirmations:

- Self
- Patient
- Agenda

Checks:

- Understanding
- Expectations
- How he feels

Opening Question:

- I got to know that you have been troubled with problem in walking
- Could you tell me more about that?
- Yes doctor, I have problem on walking, I feel like my gait is not okay

Systemic review:

What do you mean exactly by problem in walking?

- **ODPARA**:
    - Onset
    - Duration
    - Progression
    - Associations
    - Relieving factors
    - Aggravating factors
- If you sit down, are you getting difficulty standing up, like in toilet squatting?
- Find difficulty in combing your hair?

- Any fall?
- Any loss of balance when close your eyes?
- Any back pain
- Any weakness anywhere in your body?
- Any headache?
- What about sun exposure?
- Any history of bone fractures?
- Any teeth problems?
- Any pains or aches?
- Any joint pain?
- **Are you taking balanced diet?**

- Including milk and dairy products?
- **Any problem with your water work?**
- **Any loose motion?**
- **Any yellow discoloration of white of the eyes?**

Differential diagnosis of proximal myopathy

1. **Cushing's syndrome**
2. **Polymyalgia rheumatica**
3. **Hyperthyroidism**
4. **Polymyositis/ dermatomyositis**
    i. Skin rash
5. **Osteomalacia**
6. **Paraneoplastic syndrome**
    i. Any fever, weight loss, pumps and lumps
7. **Alcohol**

Past medical history:

- Any medical illness you are suffering from I should be aware of?
- Like DM and HTN

Drug History:

- Show me your medication list
- Any allergies?

Family history:

- Any significant disease runs in family?
- Any family history of similar condition?
- May I ask you private questions which are important for our discussion today:
    - Any chance you are pregnant?
    - What about your period?

Social History:

- What do you do for living?
- How these symptoms affecting you at work and driving?
- Do you smoke?
- **Do you drink alcohol?**
- How is your home condition?
- Any support needed?
- **Are you exercising?**
- **Are you getting enough son exposure?**

Surgical history:

- Any surgeries in the past?

Can I examine you?

- **Ask patient to stand**
- **Look from behind for scoliosis**
- **Look from the side for kyphosis**
    - The presence of **kyphosis** suggests metabolic bone disease i.e. **osteomalacia**.
    - **Kyphosis suggests metabolic bone disease** or **spondyloarthropathy**.

        - **Assess cervical spine mobility** to decide whether to proceed to a **metabolic bone disease'** routine', or an **ankylosing spondylitis** 'routine'.
- **Ask the patient to walk a short distance.**
- **A waddling gait**
    - This patient has a waddling gait.
    - Suggests weakness of the proximal muscles that stabilize the weight-bearing hip.
    - The pelvis drops, and the patient will lean to the weight-bearing side to maintain balance.
    - This is the **same** as the **Trendelenberg gait**.
- **Muscle tenderness** - osteomalacia
- **Proximal myopathy** - upper **limbs**.
    - Elicit this by **static testing of muscle power in the upper limbs**, 'keep your elbows out to the sides, and don't let me move them'.
    - There is evidence of a proximal myopathy in the upper limbs.
- Features of
    - **Cushing's syndrome**
        - Cushingoid facies
        - Centripetal obesity
        - Purpura
        - Striae
        - Proximal myopathy.
    - **Thyroid disease**
        - Goitre (thyroidectomy scar)
        - Thyroid eye disease
        - Lid lag
        - Tachycardia
        - Tremor
        - Proximal myopathy.
    - **Dermatomyositis**.
        - **Gottron papules** - hands
        - **Heliotrope rash** - face
- **Skeletal deformities**:
    (a) Frontal bossing of the skull
    (b) **Enlargement of the costo-chondral junction** causing **beading of the chest**
    (c) **Bilateral symmetrical bowing deformities of the long bones**
        - **Paget's disease** results in **unilateral bowing of the legs**.
        - **Bilateral bowing** can **rarely occur** but even so, it will **not** be **symmetrical**.
        - Rickets results in bilateral and symmetrical bowing of the legs
    (d) In **long bones**, the laying down of un-mineralized osteoid at the **metaphyses** leads to a **'knobbly' deformity**.

        - In the **chest wall** this leads to the **'rachitic rosary'** along the **costo-chondral junctions**, and in weight bearing limbs this causes **'bow-legs'** and **'knock knees'**
        - The diagnosis is old rickets with persistent skeletal abnormalities and proximal myopathy
- **Feel for warmth** over the **affected bones**
        - **Paget's disease** cause warm due to increased blood flow

What is your concern?

What is wrong with me doctor, why I have this difficulty in walking?

- From what you told me and after examining you , most likely you have weakness in your shoulder and hip muscles causing the problem with you gait - Gait is rhythmic stepping movements for travel which is due to adult form of rickets which causes soft bones giving the symptoms of pains, aches you have and problem with walking
- What we need to do is to run some blood tests and imaging to confirm our diagnosis which is likely due to vitamin D deficiency which is found in milk and dairy products
- We will refer you to gland doctor and bone doctor
- Will refer you to occupational therapist, physiotherapist and dietician
- Will give pain medications
- However, it may be several months before any bone pain and muscle weakness is relieved.

Questions commonly asked by examiners

What s your diagnosis?

- **Proximal myopathy** most likely due to osteomalacia – vitamin D deficiency

How you will investigate this case?

- **Basic investigations:**
        - CBC, chemistry, including calcium and phosphate
        - Inflammatory markers
- **TFT**
- **Serum cortisol**
- **Dexa scan**
- **X-ray** - long bones and pelvis and **spine**

What are the differential diagnoses of proximal myopathy?

8. Cushing's syndrome
9. Polymyalgia rheumatica
10. Hyperthyroidism
11. Polymyositis/ dermatomyositis
12. Osteomalacia
13. Paraneoplastic syndrome
14. Alcohol

What is the etiology of rickets and osteomalacia?

- Bone is normally comprised of an organic osteoid, synthesized by osteoblasts, which is mineralized by the deposition of calcium and phosphate.

- **Defective mineralization** due to calcium and phosphate leads to **osteomalacia and rickets**.
- **Osteomalacia refers to un-mineralized osteoid**, whereas **rickets** refers to the **consequent skeletal abnormalities.**
- **Rickets and osteomalacia occur together in childhood**, causing **deformity** while the **growth plates are open** and long **bones are still growing**.
- **Only osteomalacia occurs in adulthood,** after the **growth plates** have **fused**.
- **Hypocalcemic rickets** due to vitamin D deficiency, calcium deficiency or rare defects in the enzymatic conversion of 25 (OH) vitamin D to the active form 1.25 (OH) vitamin D. Vitamin D and calcium deficiency may occur due to dietary deficiency, inadequate sunlight exposure, or malabsorption.
- **Hypophosphataemic rickets** is almost always caused by renal **phosphate wasting** by renal tubular disorders such as Fanconi's syndrome. Hereditary causes of renal phosphate wasting include X-linked **Hypophosphataemic rickets** (**vitamin D-resistant rickets**), which is a specific defect in. tubular phosphate reabsorption.
- **Adult-onset osteomalacia** is the **most common cause** of osteomalacia-**in adults is vitamin D deficiency** causing **hypophosphataemia** and **secondary hyperparathyroidism**.
- Drugs that inhibit mineralization, such as **bisphosphonates** (which are used to treat osteoporosis and **aluminum**, may cause **osteomalacia**.
- **Barbiturates** also **interfere with vitamin D metabolism** and may **cause osteomalacia**.

What are the radiological features of osteomalacia?

- **Looser's zones**
  - The characteristic radiological findings of osteomalacia.
  - These are **narrow, radiolucent lines with sclerotic borders** that occur in the **pelvis or femoral neck** and are often termed **'pseudofractures'**
  - They **may represent stress fractures** that have been **repaired** with **inadequately mineralized** osteoid.
- **Reduced bone density**
  - With **thinning of the cortex**, also occurs but is a **non-specific** finding.
- **Vertebral compression fractures**
  - Occur less frequently than in osteoporosis.

What is the difference between osteoporosis and osteomalacia?

	Osteoporosis	Osteomalacia
Pathology	Decreased bone mass due to loss of osteoid and mineralization	• Decreased mineralization • Preserved osteoid
Aetiology	Low peak bone mass and increased bone resorption	Calcium, phosphate, or vitamin D deficiency
Clinical features	No clinical manifestations until fracture	• Proximal myopathy • Bone pain
Diagnosis	Low bone density as	(a) Hypocalcaemia

	measured by dual energy X-ray absorptiometry	(b) Hypophosphataemia (c) Vitamin D deficiency (d) Secondary hyperparathyroidism
Disease associations	• Post-menopausal • Thyrotoxicosis • Hypogonadism • Corticosteroid excess • Cigarette smoking	**Vitamin D deficiency** (a) malabsorption (b) dietary deficiency (c) inadequate sun exposure **Renal tubular disease**
Treatment	• Calcium • Vitamin D • Bisphosphonates • Hormonal therapies • Parathyroid hormone (PTH)	• Calcium • Phosphate • Vitamin D
* Bone density 2.5 standard deviations or more below that of young, adult controls (T-score <- 2.5)		

Can you outline the management of postmenopausal osteoporosis?

- Consider excluding secondary causes of osteoporosis.
- Less than 10% of patients have a secondary cause, however the following investigations may be indicated:
    - **Multiple myeloma**- protein electrophoresis and urine Bence-jones protein
    - **Osteomalacia**-calcium, phosphate, alkaline phsophatase, vitamin D
    - **Thyrotoxicosis**-thyroid function tests
    - **Hyperparathyroidism** (primary or secondary)-serum PTH
    - (**Male**) **hypogonadism**--serum testosterone

Therapeutic options for osteoporosis include:

- **Smoking cessation advice**
- **Calcium and vitamin D supplementation**
    - Unless deficiency has been clearly excluded.
- **Bisphosphonates**
    - Act on the osteoclast to prevent bone resorption.
    - The most common side effect is **esophagitis**, although **osteonecrosis of the jaw** has been reported with parenteral preparations.
- **Hormonal agents**
    - Hormone replacement therapy increases bone density and treats menopausal symptoms, although there is an **increased risk of breast and uterine cancer**, and of **venous thromboembolism**.
    - Raloxifene is a selective-oestrogen receptor modulator, with oestrogenic effects on bone, but anti-oestrogenic effects on the endometrium and breasts.

        - Therefore, Raloxifene **improves bone density**, **without** conferring any additional **risk of breast or uterine cancer**, although there remains an **increased risk** of **venous thromboembolism**.
- **Recombinant PTH**
        - Although PTH is **catabolic for bone** when given continuously, in intermittent **administration** it has been shown to **increase bone density**.
        - PTH is administered by **daily subcutaneous injection**.

- **NICE guidelines (2005)** for the **secondary prevention of osteoporosis** in **postmenopausal women** suggest that **bisphosphonates** should be **used initially** for the secondary prevention of osteoporosis, with **Raloxifene reserved** for patients who are **intolerant of bisphosphonates**.

How can one determine the source of an isolated, elevated serum alkaline phosphatase?

- **Most patients with an isolated rise** in **alkaline phosphatase** have **biliary disease** rather than bone disease.
- The most immediate way to differentiate these is to **measure the serum** gamma **glutamyl transpeptidase (GGT),** which is usually **elevated in biliary disease**.
- Alternatively, the **different biliary and bone isoenzymes** can be differentiated by **electrophoresis**, although this **test is not universally available**.
- Remember that the **alkaline phosphatase** is physiologically **elevated** in the **third trimester** of pregnancy, due to **placental production**

What are the causes of bossing of the skull?

- **Rickets**- in parietal and frontal bones due to the **deposition** of **un-mineralized osteoid**
- **Other causes of frontal bossing in adults include**
    (a) Congential syphilis
    (b) Acromegaly
    (c) Osteopetrosis

- **Most** of the **skeletal abnormalities of rickets correct with growth**, although they **may persist in to adulthood if the vitamin D deficiency** is severe and **uncorrected**.
- Adults may have concomitant **proximal myopathy** if there is ongoing **vitamin D deficiency**

MRCP-PACES

Brief clinical consultation

Osteoporosis

67 years old Mr. Edwardu
Joint pain

Confirmations

- Self
- Patient
- Agenda

Opening question:

- You are troubled with joint pain
- Could you tell me more about that?
  - Yes doctor, I got this joint pain and really I am suffering from it

Brief analysis of joint pain:

ODPARA

- When did it start?
- Was it sudden or gradual?
- Is it the same, worsening or improving?
- Any other symptoms associated it?
- Anything making it better?
- Anything making it worse?
- Any **stiffness**?
- Which time of day the stiffness is more?

- Which joint is affected?
- Any **trauma**
- Any high body temperature?
- Any **gravel** in water work?
- Any lumps and pumps?
- **Did you put more body weight recently?**

- Any **skin rash**
- Any **nail change**
- **Can I see it?**

Drug history:

Family history:

Social history:

- Job
- QOL
- Driving
- Smoking
- Alcohol

Can I examine you?

Could you put your both hand on pillow on your lap before I examine you?
Any joint pain before I touch you?

- **Walking aid** around the **bed side**
- **Splint** in left knee and right wrist
- **Nail –** no changes
- **Skin -** No rash.
- **Hands:**
    - **Asymmetrical bony swelling** affecting the **DIP** (**Heberden's nodes**) and **PIP** (**Bouchard's nodes**) joints of hands
    - **Squaring** of the **first metacarpophalangeal joint**
    - There is **no** evidence of **synovitis**
- **Mobility**:
    - **Assess mobility** of the **hands**, **wrists**, **elbows**, and **shoulders**
- **Knees:**
    - **Varus deformity**
    - **Palpate for warmth** with the **dorsum** of **hand**
    - **Palpate** for **tenderness** on the **joint line**.
    - **'Bulge test'** for an **effusion** - since they are likely to be small
        - Place your left hand above the knee
        - **'milk' the suprapatella bursa** towards the knee
        - Look for a bulge in the **medial patella fossa**.
    - Feel the **crepitus**
        - Place **palm on the knee joint**, feeling for **crepitus during passive movement of the knee**
- **Gait:**
    - Can I see you **walking** if possible and if causing no pain?
    - The **gait is antalgic**
    - **Waddling gait =**
        - **Trendelenberg's sign** is positive
        - Suggesting **proximal weakness of hip stabilizers**
- **Observation chart** to check **temperature**

What is your concern?

- From what you told me and after I examined you most likely you have a condition called osteoarthritis affecting your hands and knee
- It causes the symptoms which you have

- What we need to do is to arrange some blood tests, imaging and will refer you to joint doctor, physiotherapist, occupational therapist to give the best plan of care for your condition
- I advise you to lose weight and to do regular exercise
- Is that okay with you?
- **Do you have any other concern?**

Questions commonly asked by examiners

How would you distinguish osteoarthritis from rheumatoid arthritis?

- Patients with **OA** have **pain** that is **worse on movement** and **relieved by rest**.
- Whilst they may have a degree of **morning stiffness**, this is **typically less than an hour, unlike RA**.
- Stiffness may occur following a period of activity (**'gelling'**), but this is **less prominent** than the stiffness seen in RA.
- In **OA** the disease is **asymmetrical**, and involves the **DIP** joints, **unlike RA** which is typically **symmetrical** and **spares the DIP joints**.
- Furthermore, OA has distinct radiological features.

What are the radiological features of osteoarthritis?

1. **Joint space narrowing**
2. **Marginal osteophytes**
3. **Subchondral sclerosis**
4. **Subchondral cyst formation**

- Radiological findings are poor predictors of the degree of symptoms in a particular patient.

What are the principles of management of osteoarthritis?

- **General measures**
    - Patient education-weight loss
    - Physiotherapy-to prevent disuse atrophy, particularly of the quadriceps
    - Occupational therapy
- **Pharmacological treatment**
    - **Analgesics**
        - **NSAIDs**
    - **Corticosteroids**
        - **Intra-articular steroid** injections for single troublesome joints, although **no more than 4 times per year**.
        - There is no role for systemic steroids.
- **Non-pharmacological treatment**
    - **Arthroscopy**
        - This is only useful if there is a mechanical defect that can be debrided
    - **Surgery**
        - **Osteotomy** for a malaligned hip or knee joint
        - **Total joint replacement** for end-stage disease

Clinical notes

- Although t here is less deformity and disability in osteoarthritis (OA), and fewer systemic signs, the candidate should adopt a similar routine for examination of the hands as outlined in Rheumatoid Arthritis.
- Remember to **ask about joint pain before shaking the patient's hand** or examining.
- Before touching t he patient, look for **walking aids** or **carpal tunnel splints**.
- Now, gently place the patient's hands on a pillow, and look at the pattern of joint involvement.
- **DIP** involvement suggests **OA**, **psoriatic** arthropathy, or **gout**.
- Remember to look for **nail changes**, and examine the hairline for **rash** and **earlobles** for **tophi**.
- **Bony swellings** at the **DIP** (**Heberden's nodes**) and **PIP** (**Bouchard's nodes**) joints are characteristic of OA
- These are tender **osteophytic extensions** of the joint, unlike **tophi** which are **non-tender urate collections** in the soft tissues, or **rheumatoid nodules** which are **non-tender inflammatory lesions**.
- The **first MCP joint** is commonly involved in OA **particularly** in **females**.
- Enlargement of this joint result in a **'squared'** appearance of the **hand**.
- Remember to **assess mobility** of the hands, wrists, elbows, and shoulders
- Now **look briefly at the knees**, noting any **deformity**
- **Varus deformity** is more common in OA since the **medial compartment** of the knee is **most frequently affected**.
- **Palpate for warmth** with the **dorsum of your hand**, and palpate for **tenderness** on the joint line.
- Now use the **'bulge test'** to look for an **effusion**, since they are likely to be small in the MRCP (PACES) examination.
- Place your left hand above the knee and **'milk' the suprapatella bursa** towards the knee, looking for a bulge in the **medial patella fossa**.
- Now place your **palm on the knee joint**, feeling for **crepitus during passive movement of the knee**.
- An **antalgic gait** or **‘limp’** implies a **painful joint**, whereby the phase of the **gait** is **shortened to alleviate pain** on the weight-bearing side.
- A **waddling** or **Trendelenberg’s**, gait may also be present if there is **bilateral weakness of hip stabilizers**.
- Trendelenberg's sign is positive if, when standing on one leg the **pelvis drops on** the **non-weight bearing leg**, **implying weakness of t he hip stabilizers** on the **weight-bearing side.**

Explaining Osteoarthritis

- It is a medical condition in which there is affection of joints which become stiff and painful and causing problems when moving the joints
- Some people also have symptoms such as swelling - tenderness - grating or crackling sound when moving the affected joints
- limited range of movement in your joints
- weakness and loss of muscle bulk
- For some people, the symptoms can be mild and may come and go.
- Other people can experience more continuous and severe problems which make it difficult to carry out everyday activities
- As part of normal life, your joints are exposed to a constant low level of damage. In most cases, your body repairs the damage itself and you do not experience any symptoms.
- But in osteoarthritis, the protective cartilage on the ends of your bones breaks down, causing pain, swelling and problems moving the joint.
- Bony growths can develop, and the area can become red and swollen.
- **The exact cause is not known**, but several things are thought to increase your **risk of developing osteoarthritis, including:**
    - Other joint problems
    - Joint injury
    - Obesity
    - Family history
    - Old age

Treating osteoarthritis

- Osteoarthritis is a long-term condition and **cannot be cured**, but it doesn't necessarily get any worse over time and it can sometimes gradually improve.
- A number of treatments are also available to **reduce the symptoms**.
- Mild symptoms can sometimes be managed with **simple measures including**:
    - **regular exercise**
    - **losing weight if you're overweight**
    - **wearing suitable footwear**
    - **using special devices** to reduce the strain on your joints during your everyday activities
- **If your symptoms are more severe**, you may need additional treatments such as **painkillers** and a **structured exercise** plan with a **physiotherapist**.
- In a small number of cases, where these treatments haven't helped or the damage to the joints is particularly severe, **surgery** may be done to repair, strengthen or replace a damaged joint

Preventing osteoarthritis

- It's **not possible to prevent osteoarthritis altogether**.
- However, you may be able to minimize your risk of developing the condition by avoiding injury and **living a healthy lifestyle.**

There's no cure for osteoarthritis, but the condition does not necessarily get any worse over time.
There are a number of treatments to help relieve the symptoms.

- The main treatments for the symptoms of osteoarthritis include:
- **lifestyle measures** – such as maintaining a healthy weight and exercising regularly
- **medication** – to relieve your pain
- **supportive therapies** – to help make everyday activities easier
- In a few cases, where other treatments have not been helpful, **surgery** to repair, strengthen or replace damaged joints may also be considered.

Living with osteoarthritis

- As osteoarthritis is a **long-term condition**
- It's important you receive **support** to help you cope with any issues such as reduced mobility, and advice on any necessary **financial support**

Lifestyle changes

Exercise

- Exercise is one of the most important treatments for people with osteoarthritis, whatever your age or level of fitness.

Losing weight

- Being overweight or obese often makes osteoarthritis worse, as it places extra strain on some of your joints.

Pain relief medicines

- Sometimes a combination of therapies, such as painkillers, exercise and assistive devices or surgery, may be needed to help control your pain.
- The main medications used are below.
    - **Paracetamol**
    - **NSAIDs**
    - **Opioids**
    - **Capsaicin cream**
    - **Steroid injections**
- **Supportive treatments**
    - **Transcutaneous electrical nerve stimulation (TENS)**
    - Transcutaneous electrical nerve stimulation (TENS) uses a machine that sends electrical impulses through sticky patches, called electrodes, attached to the skin.
    - This may help ease the pain caused by your osteoarthritis by numbing the nerve endings in your spinal cord which control pain.

    - Treatment with TENS is usually arranged by a physiotherapist or doctor, who can advise you on the strength of the pulses and how long your treatment should last.
- **Hot or cold packs**
    - Applying hot or cold packs to the joints can relieve the pain and symptoms of osteoarthritis in some people.
    - A hot-water bottle filled with either hot or cold water and applied to the affected area can be very effective in reducing pain.
- **Assistive devices**
    - If osteoarthritis is causing mobility problems or making it difficult to do everyday tasks, several devices could help.
    - We may refer you to a physiotherapist or an occupational therapist for specialist help and advice.
    - If you have osteoarthritis in your lower limbs, such as your hips, knees or feet, your physiotherapist or occupational therapist may suggest **special footwear** or **insoles** for your shoes.
    - **Footwear with shock-absorbing soles** can help relieve some of the pressure on the joints in your legs as you walk.
    - **Leg braces** and supports also work in the same way.
    - If you have osteoarthritis in your hip or knee that affects your mobility, you may need to use a **walking aid**, such as a **stick** or **cane**.
    - Hold it on the opposite side of your body to your affected leg so that it takes some of your weight.
    - A **splint** (a piece of rigid material used to provide support to a joint or bone) can also be useful if you need to rest a painful joint. Your physiotherapist can provide you with a splint and give you advice on how to use it correctly.
    - If your hands are affected by osteoarthritis, you may also need assistance with hand-operated tasks, such as turning on a tap. **Special devices**, such as **tap turners**, can make performing these tasks more manageable. Your occupational therapist can give you help and advice about using assistive devices in your home or workplace.
- **Manual therapy**
    - Not using your joints can cause your muscles to waste and may increase stiffness caused by osteoarthritis.
    - Manual therapy is a technique where a physiotherapist uses their hands to stretch, mobilize and massage the body tissues to keep your joints supple and flexible.
- **Surgery**
    - Surgery for osteoarthritis is only needed in a small number of cases where other treatments haven't been effective or where one of your joints is severely damaged.
    - If you need surgery for osteoarthritis, your GP will refer you to an **orthopedic surgeon**.

- Having surgery for osteoarthritis may greatly improve your symptoms, mobility and quality of life.
- There are several different types of surgery for osteoarthritis.

- **Joint replacement**
  - Joint replacement, also known as an arthroplasty, is most commonly done to replace hip and knee joints.
- **Joint fusing**
  - If joint replacement is not suitable for you, your surgeon may suggest an operation to fuse your joint in a permanent position, known as an arthrodesis.
  - This means your joint will be stronger and much less painful, although you will no longer be able to move it.
- **Adding or removing some bone around a joint**
  - If you have osteoarthritis in your knees but you're not suitable for knee replacement surgery, you may be able to have an operation called an osteotomy. This involves your surgeon adding or removing a small section of bone either above or below your knee joint.
  - This helps realign your knee so your weight is no longer focused on the damaged part of your knee. An osteotomy can relieve symptoms of osteoarthritis, although you may still need knee replacement surgery eventually.
- **Complementary and alternative therapies**
  - Some people with osteoarthritis try complementary or alternative therapies – such as acupuncture and aromatherapy – and find them helpful.
  - However, there's a lack of medical evidence to suggest they're effective and they generally are not recommended by the National Institute for Health and Care Excellence (NICE).
- **Nutritional supplements**
  - A number of nutritional supplements have been used to treat osteoarthritis in the past, including chondroitin and glucosamine.
  - GPs no longer prescribe chondroitin and glucosamine on the NHS because there’s no strong evidence that they are effective as a treatment.
  - Generally, supplements can be expensive and NICE recommends that they should not routinely be offered on the NHS.

Rubefacients

- Rubefacients are available as gels and creams that produce a warm, reddening effect on your skin when you rub them in. Several rubefacients have been used to treat joint pain caused by osteoarthritis.
- However, research has shown that rubefacients have little effect in improving the symptoms of osteoarthritis and NICE therefore does not recommend their use.
- Living with osteoarthritis:

With the right support, you can lead a healthy, active life with osteoarthritis

The condition does not necessarily get worse

- A good diet and regular exercise will help keep muscles strong and control your weight, which is good for osteoarthritis and also has other health benefits.

Taking your medicine

- It's important to take your medicine as prescribed, even if you start to feel better.

Regular reviews

- Because osteoarthritis is a long-term condition, you'll be in regular contact with your healthcare team.

Work and money

- If you have severe osteoarthritis and are still working, your symptoms may interfere with your working life and may affect your ability to do your job.
- If you have to stop work or work part time because of your arthritis, you may find it hard to cope financially.
- You may be entitled to 1 or more of the following types of financial support

MRCP-PACES

Brief clinical consultation

Back pain – Paget's disease of bone

You are SHO in medical OPD
Mr. Kumar 55 years old
Referred with history of **back pain**
Please see and advice

ODPARA

- Any specific time
- All the time
- **3S:**
    - **Stiffness**
    - **Site**
    - **Severity**
- Pain - **mechanical**
- Increased with movement
- **Red flag:**

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1. **Cancer:**
    i. Loss of weight
    ii. Loss of appetite
    iii. History of nasty growth
    iv. Lumps and pumps
2. **Cord compression:**
    - Weakness
    - Numbness
    - Loss of control of sphincters

- **Local cause:**
    - **Trauma**
    - **Deformity**
    - **Recent travel**
    - **Fever**
- Other joints
- Weight change
- Skin changes
- **Hearing problem**
    - Last two months
    - Seek medical advice

    - Hearing aid

Examinations:

- Back
- Tenderness lower back
- Leg bowing

Concern:

What's wrong with me?

- Most likely you have a condition called Paget's disease of the bone in which the normal process of repair and renewal of bone are disturbed
- Can affect other organs like hearing and heart

Is it cancer?

- No, it is not a cancer
- Rarely have risk of cancer
- Less than 1%

Social:

- Job
- Advice you to stop smoking
- Alcohol

What are positive findings

- There **bossing of skull**
- **Hearing aid**
- **S3 gallop**
- **Bowing of legs**
- Edema - look to face
- **Localized swelling**
- **Kyphosis**, deformity of back
- Check **tenderness press lower back** inform patient

Diagnosis:

- Paget's disease of the bone

Differential diagnoses:

1. Osteoarthritis - age
2. Spondylitis of back

Investigations:

- **A- Blood tests:**
    - CBC
    - Calcium, normal
    - Alkaline phosphatase - high, clue
    - PTH
    - Phosphorus

- **B- imaging**
    - X ray back
    - **Skull cotton wool pattern, sclerotic**
    - **Isotope bone scan:** Extent of **disease and activity**
- **Urine or serum for hydroxyproline marker of turn over**

Treatment:

- **Non pharmacologic:**
    - Physiotherapist
    - Occupational therapist
    - MDT ortho, ENT
- **Pharmacological:**
    - Bisphosphonate
    - Pain killer

MRCP-PACES

Brief clinical consultation

Post Bariatrics surgery hand pain

You are a doctor in **GIM clinic**
44-year-old Mrs. Mary
Having **pain in hands**
Please see her

Opening question

- I got to know that you are suffering from pain in your hands
- Could you tell me more about that?

Analysis of hand pain:

ODPARA

- Onset
- Duration
- Progression
- Association
- Worsening factors
- Relieving factors

- **Where this pain exactly**
- Any pain anywhere else?
- Any time of the day this pain is more?
- In which
- Do you need to shake hands to sooth this pain?
- Any skin rash
- Any high body temperature
- Any weight changes?
- Yes, I have weight increment

Screen about weight increment:

- Is it intentional?
- How many kilos did you put and over how long?

- Where did you exactly put on weight more in your body?
    - All over doctor
- **What about your diet, is it balanced?**
- Are you exercising?

Causes:

- **Pregnancy:**
    - Any chance of Pregancy
- **Hypothyroidism:**
    - Neck swelling
    - Weather preference
- **Acromegaly:**
    - Change in face, change in hands and feet
- **Cushing's**
    - Thinning of the skin
    - Skin bruises
- **Obesity association:**

1. **Metabolic syndrome:**
    - Are you diabetic?
    - Is it controlled?
    - What is the last 3-month blood sugar reading?
    - Any weakness
    - Any loss of sensation
    - Any blurring of vision
    - What about your water work?
    - Any history of high Cholesterol
    - Any history of high BP?
2. **Depression:**
    - What about your mood?
    - Biliary colic:
        - Tummy pain
3. **GERD:**
    - Acid brash sensation
    - Regurgitation of food
    - Chest pain
4. **OSA:**
    - Any morning headache

Endurance

- Feeling **non-refreshed by sleep**
- **Snoring observed by others**

5. **OA:**
   - Knee pain
   - Back pain

Drug History:

- Any allergies
- Show me your medication list
- **Medications associating increase weight:**
  - **Corticosteroids**
  - **Antidepressants**
  - **Antipsychotics**

Family History:

- Any significant illnesses?
- Obesity

Past Medical History:

- Any high blood sugar or high BP?
- Any overweight during childhood?
- Any history of surgery?
  - Yes, I underwent weight reducing surgery
  - When was that?

Social History:

- What do you do for living?
- How the hand pain affecting you at work and in your daily activity?
- How you cope with your weight change at work?
- Is it affecting you in daily activity?
- Do you smoke?
- Do you drink alcohol?

Can I examine you?

- Obese patient
- No xanthelasma
- **Neck** parathyroid **surgery**?
- Chvostek sign
- Trousseau sign

Endurance

- **Abdominal striae**
- **Excess skin folds indicative of rapid weight loss.**
- Scars consistent with laparoscopic port insertion in the peri-umbilical area and upper abdomen
- No lipodystrophy
- Hepatomegaly
- Finger pulp blood sugar checking scars
- CVS: No chest wall scar
- **Knees- OA**
- **Test for proximal myopathy**
- **Body mass index**

What is your concern?

Why I have this pain?

- From what you told me and after examining you, most likely you have
- reduced salt in your body - called **calcium**
- It is related to the surgery you did for your weight reduction
- What we need to do is to do some blood tests and imaging to confirm the diagnosis
- Will refer you to gland doctor and dietician for best plan of management and will give you pain medicine
- Is that okay with you?

What is your diagnosis?

- **Vitamin D deficiency induced hypocalcemia**

What are your differential diagnoses?

- **Of obesity, centripetal, or abdominal fullness?**
    1. Cushingoid
    2. Hypothyroidism
    3. Ascites
- **Of the laparoscopic procedure?**
    - Cholecystectomy
    - Bariatric surgery
        - **restrictive procedure:**
            1. gastric banding
            2. sleeve gastrectomy
        - **bypass procedure**

1. Roux-en-Y gastric bypass
2. Nissen's fundoplication

How you will investigate this case?

- **Basic investigations**
  - Chemistry including calcium
  - Phosphorus
  - Albumin
  - RFT
  - PTH
- ECG
- Vitamin D Level

How you will investigate any obesity case?

- **Body mass index (BMI)**
  - Weight in kilograms divided by the square of height in meters
- **Waist circumference:**
  - It is prudent to investigate the possibility of metabolic syndrome; a clustering of risk factors for the development of severe ischemic cardiac disease and type 2 diabetes:
    1. Insulin resistance – measure fasting glucose
    2. Dyslipidemia with elevated triglycerides, low HDL and increased intra-abdominal adiposity
    3. Hypertension
- **Note**
  - In unexplained obesity consider the need to rule out rare causes of weight gain including:
    - Hyperinsulinism due to pancreatic cancer
    - Craniopharyngioma

How are you going to manage obesity?

- **Management plan of obesity:**
  - **Dietary and exercise advice**
  - **Dietitian referral**
  - **Medication:**
    1- Orlistat
    2- GLP-1 receptor agonists in those with diabetes
  - **Cognitive behavioral therapy**

endonote

- **Bariatric surgery**
  - Most bariatric surgery is performed laparoscopically.
  - It is generally indicated where all reasonable efforts have been made to exhaust alternative methods of weight loss and where there are no concerns about compliance with subsequent dietary requirements, mental health concerns or substance misuse.
  - A BMI > 40, or >35 with a serious complication such as diabetes or ischemic heart disease, represents objective indications.
  - Metabolic risk factors should be treated aggressively with diet and exercise advice, metformin where appropriate and optimization of modifiable cardiac risk factors with hypertension control and a low threshold for statin use.

endurance

MRCP-PACES

Brief clinical consultation

Psoriatic arthritis

Scenario:

You are SHO in rheumatology clinic
Mr. Edwardo is 40-year-old man
Complaining of joint pain

Confirmations:

- Self
- Patient
- Agenda

Opening question:

- You got troubled with joint pain
- Could you tell me more about that?
  - I have been referred to the rheumatology outpatient clinic with painful joints affecting both hands.

Analysis of joint pain:

ODPARA:

- **How long** has the joint discomfort been present?
- Any **swelling**?
- **Which joints** are affected?
- Any **other joints** affected apart from those?
- **Symmetrical** versus **asymmetrical**
- Was it **sudden** or **gradual**
- Is it the **same**, **improving** or **worsening**?
- Have symptoms been **constant** or **intermittent**?
- Are there any **exacerbating** or **relieving** factors?
  - Prolonged sun exposure may precipitate or alleviate
- Are the symptoms worse in the **morning or evening**?
- What is the effect of joint movement and exercise?

- Any time of the day when pain is at the worst?
- Any medicines given?
- Were they provide relief of pain?
- Are you compliant to them?
- Any deformity
- Are they feeling warmer
- Any change in color of joints?
- **Any stiffness**
  - Yes
  - What time this **stiffness** is more?
  - In the **morning**
- Any difficulty in making close fist or straightening our fingers?
- **Any Rash?**
  - Where?
  - Itching?
  - Is it painful
- **Any nail changes**
- High body temperature
- Any recent throat infection – **guttate** psoriasis and **streptococcal** infection

Anterior uveitis- eye redness

Associated hyperuricemia:

- Any gravels in your water work?
- Any pumps in your skin or in your ear lobes?

Differential diagnosis of joint pain:

- **foot pain** or back of foot pain - enthesitis - **Enthesitis**: Achilles tendon – (**Achilles' tendonitis**) attachment or plantar fascia to the calcaneus and **plantar fasciitis** (especially if bilateral)
- Any **redness of eyes** - RA
- Any change in bowel habit - **bloody diarrhoea** - IBD
- **Rash:**
  - vasculitis, SLE, psoriasis
- **Back pain** - ankylosing spondylitis
- **Orogenital ulcers**
  - SLE
  - Behçet's disease

endurance

- reactive arthritis
- **Genitourinary** symptoms
  - Reactive arthritis
  - Gonococcal arthritis

Triggers:

- Stress
- Alcohol
- Strep infection
- Drugs

Past medical history

- Rheumatoid arthritis
- Osteoarthritis
- Psoriatic arthropathy.
- Ankylosing spondylitis
- SLE
- Gout
- Pseudogout (enquire about related conditions*)
  - * Haemochromatosis. hypothyroidism, hyperparathyroidism, acromegaly, diabetes.

Social History:

- **What effect is this having on your daily life?**
  - opening the front door
  - opening jars of food
  - dressing
- Over the last month, I have not been able to work due to debilitating symptoms
- **Psychological impact**
- Alcohol
- Smoking
- **Stress**
- **Welfare:**
  - Home and work-place **adaptation**
  - Disability **benefit**
  - Support group
  - DMARDS, anti- TNF: monitor CBC and LFTS
  - **Teratogenicity** in women - contraception

Endurance

Drug history:

- Allergies
- Review the **analgesic** medications
- Enquire about **compliance**
- **Taliban+**
    - **Tetracycline**
    - **ACEI**
    - **Lithium**
    - INF
    - Beta-Blockers
    - NSAIDs
    - Calcium Channel Blockers – Captopril
    - **Alcohol**
    - **Hydroxychloroquine**

Can I examine you?

- **Examine the joints**
    - Establish the distribution of joint involvement
    - Distal interphalangeal joint involvement
    - **Symmetrical** versus **asymmetrical**
    - Look for **deformities**
        1. **Asymmetrical oligoarticular** arthritis
        2. **Symmetrical polyarthritis** - commonest type and like rheumatoid arthritis
        3. **Distal interphalangeal** involvement
        4. **Arthritis mutilans** with subluxation and ulnar deviation at the MCP joints.
        - **Dactylitis** with '**sausage' digits**
    - Are the joints **warm** to touch?
    - Warmth suggests active inflammation.
    - **Inspect overlying skin.**
    - Erythema suggests active inflammation or infection.
- **Function:**
    - assess function by asking the patient to **unbutton** their **shirt** or to **pick a coin** off a flat surface
- **Expose skin:**
    - **White scaly** above **salmon pink plaques**

endurance

- Reddish plaques with well-defined edges and silvery white scales
- On **extensor** surface especially elbows, knees
- **Symmetrical**
  - Scalp
  - Behind the ears
  - Natal cleft - Buttocks for Rash (Auspitz Sign)
  - Navel, umbilicus
  - Sub mammary region
  - Nape of neck
  - Hairline
- Surgical scars (Koebner's phenomenon) – site of trauma
- **Inverse psoriasis** is a variant of psoriasis that appears on the **flexor surfaces** and affects **intertriginous** areas, i.e. **axillae**, **inguinal folds, infra-mammary creases** with **minimal scaling**.

- **Guttate:**
  - Droplets, limb, and trunk
- **Palmoplantar pustulosis:**
  - On palm and soles
- **Erythrodermic:**
  - Generalized erythema and scales
- **Examine the nails -** involved in **80%** of psoriatic arthritis
  1. Nail pitting
  2. Transverse ridging
  3. Onycholysis - is the separation of the nail plate from the nail bed.
  4. Oil spots (pathognomonic)
  5. Subungual hyperkeratosis
- **Back for any restriction of movement** or presence of **sacroiliitis**
  - **Sacroiliitis** is often asymmetrical in psoriatic arthritis, whereas it is almost always bilateral in patients with ankylosing spondylitis.
- Examined for **systemic associations of psoriasis**:
  - **Musculoskeletal**: gout (psoriasis is associated with hyperuricaemia)
  - **Cardiovascular**: aortitis and aortic regurgitation

- **Respiratory**: apical lung fibrosis (rare)
- **Eyes**: conjunctivitis, uveitis

What is your concern?

My mother has rheumatoid arthritis and is left with considerable deformity of the hands and I have been particularly concerned that this may be rheumatoid arthritis and me too will be left with a permanent disability

- From what you told me and after I examined you, most likely you have a condition called **psoriatic arthropathy**
- And due to defect in body own defense system attacking skin and joints causing the symptoms which you have
- Psoriatic arthropathy is different to rheumatoid arthritis and is often not associated with severe joint deformities and disability that can otherwise occur in rheumatoid arthritis.
- What we need to do now is to arrange some blood tests and imaging to confirm the diagnosis and will refer you to joint doctor, skin doctor, social worker, physiotherapist, and occupational therapist
- Will give you pain medication for the time being to relief your joint pain till you will be assessed by the joint pain
- **Is that okay with you?**
- **Do you have any other concerns?**

Can this be treated effectively?

- Methotrexate and TNF-inhibitors are highly effective treatments for Psoriatic Arthritis, and one would expect the patient to remain in employment if treated appropriately and effectively.

Will I have to give up my job?

Will my children develop this disease?

- As **Psoriatic Arthritis** can be associated with **HLA B27** there is an increased chance of offspring developing the disease i.e. a **50-fold** increase if a **first degree -degree** relative has the disease.

Will I have to take medication for the rest of my life?

- Psoriatic Arthritis very **rarely goes into spontaneous remission** and therefore most patients will remain dependent on medication to control their arthritis.

Examiners' questions

Present your findings

- On examination of this gentleman, there is an **asymmetrical arthropathy** of the hands mainly involving the distal interphalangeal joints
- There is **nail pitting**, **onycholysis**, **transverse ridging**, and **subungual hyperkeratosis**.
- In addition, there are **well-defined erythematous plaques** with **silvery white scales** over the **extensor surfaces**.

What is your diagnosis?

- The diagnosis is psoriatic arthropathy and psoriasis

What are the types of psoriatic arthropathy?

1. Symmetrical deforming polyarthropathy
2. Arthritis mutilans
3. Predominance for DIPS
4. Asymmetrical large joint oligoarthropathy
5. Spondyloarthropathy'

What are the differential diagnoses of symmetrical deforming polyarthropathy

1. **Rheumatoid** arthritis
2. **psoriatic** arthropathy
3. **Jaccoud's** arthropathy

What are the differential diagnoses of asymmetrical arthropathy

1. Gout
2. Osteoarthritis

What are the differential diagnoses of arthropathy of the small joints of the hands?

(a) Rheumatoid arthritis

(b) Seronegative arthropathies:

- Psoriatic arthropathy
- Ankylosing spondylitis
- Reactive arthritis
- Enteropathic arthritis

(c) **Arthropathy related to other rheumatological diseases:**

- Scleroderma
- SLE

- Sarcoidosis
- Vasculitis

(d) Osteoarthritis
(e) Gout
(f) Pseudogout
(g) Viral infections
(h) Malignancy

What are the differential diagnoses of dactylitis?

1. Gout
2. Reactive arthritis
3. Sarcoidosis.

What are the differential diagnoses of Oligoarthropathy?

1. **Reactive** arthritis
2. **Sarcoidosis**
3. **Gout**

How you will investigate this case?

No specific diagnostic tests are available.

Basic investigations:

- **Blood tests**
  - FBC – anemia
  - RFT- NSAIDs
  - liver function test (LFT)*
  - Inflammatory markers (CRP and ESR) – may be normal
  - Rheumatoid factor is usually negative although may be positive in a small number of cases
  - Testing for ANA is of no diagnostic benefit.
  - Autoimmune profile (if suspecting autoimmune disease)
- **X-ray of the joint(s)**
  - Demonstrate bony erosive disease
  - In contrast to rheumatoid arthritis, there is minimal juxtaarticular osteopenia.
    - Pencil in Cup Sign
    - Narrow Joint Space
    - Distal Joint Affection
- **MRI Sacroiliac Joint**
- **HLA B27**

- Skin biopsy or scraping - clubbed rete pegs

How are you going to manage this case?

General measures

- Patient education
- Emolients
- Remove triggers
- Anti- pruritic
- **Lifestyle advice:**
  - ✓ **cardiovascular disease** and **diabetes** which are associated with chronic psoriasis.
- **Multidisciplinary input**
  - ✓ Occupational therapy
  - ✓ Physiotherapy

Pharmacological treatment

- **Analgesics**
  - **NSAIDs** (in some patients NSAIDs may worsen psoriasis)
- **Corticosteroids**
  - **Intra-articular steroid** injections for **single** troublesome **joints**.
  - Avoid **systemic steroids** since skin disease may **flare** on steroid withdrawal.
- **DMARDs**
  - ➢ **methotrexate**, **sulphasalazine** and **cyclosporin** are the most used DMARDs.
  - ➢ They are **effective in treating skin symptoms**, and the symptoms of **peripheral arthritis but not axial symptoms**.
  - ➢ Moreover, no studies have evaluated their efficacy in preventing or retarding progression of joint damage.
  - ➢ **Gold** and **penicillamine** may be useful but **few controlled studies** have been **done**.
  - ➢ **Cyclosporin** may also have a place in **refractory disease**.
- **Biological therapy**
  - ➢ **anti TNF-a therapy** with **etanercept, infliximab**, and **adalimumab** has been shown to **improve skin disease**, **joint disease**, and **disability** in psoriatic arthropathy.
- **Antimalarials**

- **Chloroquine** and **hydroxychloroquine** were **previously avoided** due to concerns about **worsening psoriasis** and precipitating exfoliative dermatitis.
- Recent case-controlled studies have not confirmed this association, although these agents are still **rarely used**.

Treatments of the skin disease:

- Ultraviolet (UV) light
- Coal tar
- **Dithranol**
- **Local steroids**
- **Calcipotriol**
- Psoralen and UVA light (**PUVA**)
- **Systemic therapy for skin disease:**

  - **Systemic treatment** with **acitretin** (a **retinoid**) or **antimetabolites** (methotrexate, azathioprine, hydroxyurea), because of their side-effects, should be reserved **for severe widespread disease unresponsive to topical measures**
  - The **DMARD sulphasalazine** is helpful for the arthritis, but not skin disease
  - **methotrexate**, which is effective against both the skin disease and the arthritis.
  - **Leflunomide** is also an effective treatment for the **arthritis** and to a **lesser** extent for the **skin disease.**
  - **Steroids** are used with caution as a significant flare of skin disease usually occurs on their withdrawal.
  - **Local cortisone injections** are highly effective for **enthesitis**.
  - If the patient's disease is **severe** enough, then **anti-TNF blockers** can be prescribed, which are highly effective in controlling the joint and skin involvement.

What are the patterns of joint involvement seen in psoriasis?

1. **Spondyloarthropathy - sacroiliitis**: this differs from ankylosing spondylitis, most notably in that the syndesmophytes tend to arise from the **lateral and anterior surfaces** of the vertebral bodies and not at the margins of the bodies
2. **Rheumatoid-like pattern** (**symmetrical**, persistently **seronegative**).
3. **Arthritis mutilans** (destructive – shortened fingers, with **resorption/telescoping** of joints).

4. **DIP** joint involvement.
5. **Oligoarthritis** (asymmetrical, often with massive effusions).

What are the radiological features of psoriatic arthritis?

- 'Fluffy' **periostitis**
- **Destruction** of small joints
- '**Pencil and cup'** appearance, **osteolysis** and **ankylosis** in arthritis mutilans
- **Non-marginal syndesmophytes** in spondylitis

What is the prognosis?

- **Deforming** and **erosive arthritis** is present in 40% of cases and **11% are disabled** by their arthritis

How can you differentiate between Psoriatic Arthritis and RA?

The following favor a diagnosis of Psoriatic Arthritis rather than RA:

- **Asymmetry**.
- **Negative rheumatoid factor** and **anti-CCP** antibodies.
- Presence of **nail changes**.
- **Dactylitis** (**inflammation** of **entire finger or toe**, leading to **sausage** digits).
- A **family** or **personal history** of psoriasis.

Do you know any HLA associations of psoriatic arthritis?

- **HLA B38/B39** is associated with **peripheral distal arthritis**.
- **HLA DR4** with a **rheumatoid distribution** subtype.
- **HLA B27** with the **sacroiliitis/spondyloarthropathy** form.

Aside from the skin lesions, which features distinguish the other spondyloarthropathies from psoriatic arthropathy?

- **Psoriatic arthropathy** is classified with the spondyloarthropathies because of the presence of
    1. **spondylitis in up to 40% of patients**

2. **extra-articular features** common to the spondyloarthropathies (iritis, colitis, aortic root inflammation)
3. **HLA-827.**

- However, **psoriatic arthropathy** can be **distinguished** from the other spondyloarthropathies by the
    1. presence of **peripheral arthritis**
    2. **asymmetry of spinal involvement**
    3. **less pain**.

What" do you understand by the term 'enthesitis'?

- Enthesitis refers to **inflammation of the site of insertion of ligaments**, tendons, joint capsule, or fascia to bone.
- Enthesitis is relatively **specific for spondyloarthropathy**, and the **most common sites** of inflammation are:
    1. the insertion of the Achilles tendon (**Achilles tendonitis**)
    2. the insertion of the plantar fascia ligament to the calcaneus (**plantar fasciitis**).

What" do you understand by the term 'Dactylitis'?

- Dactylitis is characterized by **'sausage-like' swelling** of the **finger** or toe, due to **inflammation of the tendon sheath** and **soft tissues**.
- Dactylitis is a **feature of spondyloarthropathy** but is **not specific** and may also be caused by tuberculosis, syphilis, sarcoidosis, and sickle-cell disease.
- **Fusiform swelling of the digits** may also occur due to soft tissue swelling in **gout**.

What are the indications for anti-TN Fa drug therapy?

RA:

- Infliximab, Etanercept, Adalimumab
- Active rheumatoid arthritis not responding to methotrexate and one other DMARD

Juvenile idiopathic arthritis

- Etanercept
- Children age d 4--17 years with at least 5 joints affected
- Poor response to, or who cannot tolerate methotrexate

Psoriatic arthropathy

- Etanercept (1st line), Infliximab
- ≥3 tender joints and ≥3 swollen joints
- Poor response to ≥2 disease modifying anti-rheumatic drugs

Psoriasis

- Infliximab, Adalimumab, Etanercept
- Severe psoriasis refractory to ≥2 systemic treatments and photochemotherapy

Ankylosing Spondylitis

- Adalimumab**,** Etanercept (infliximab is no longer recommended)
- Active spinal disease not responding to ≥2 NSAIDs

Crohn's Disease

- Infliximab
- **Severe** and active Crohn's disease, or **fistulating** Crohn's disease, in patients **unable to tolerate** or **refractory to immunomodulators**, and in whom **surgical** intervention is **inappropriate**.

What are the adverse effects of anti-TN Fa drug therapy?

- **Serious infections (e.g. tuberculosis)-incidence 3.6%,** odds ratio 2.0
- **Hematological malignancy**-incidence **0.9%,** odds **ratio 3.3**
- **Nausea**
- **Hypersensitivity**
- **Worsening heart failure**
- **Hematological abnormalities**
  - Anemia
  - Leucopenia
  - Thrombocytopenia
  - aplastic anemia

What are the contra-indications for anti-TN F- α drug therapy?

- **Pregnancy** and **breast-feeding**
- **Active bacterial infection**

- **Active tuberculosis**
    - requires 2 months of anti-tuberculous therapy before anti-TNF-α therapy.
    - Latent tuberculosis (tuberculin testing may be falsely negative due to immunosuppression so patients with risk factors should receive isoniazid for 6 months alongside anti-TNF-α therapy) 2
- **Septic arthritis** in previous 12 months
- **Congestive cardiac failure**
- **Demyelinating disease**

What is the link between psoriasis and psoriatic arthropathy?

- There is no evidence to suggest a link between any subtype psoriasis or severity of psoriasis with psoriatic arthropathy.
- **Psoriatic arthropathy can occur with minimal skin involvement**.
- In 20% of cases, the arthropathy precedes the onset of psoriasis, in some cases by up to 20 years.
- Similarly, psoriasis may be present without evidence of arthropathy, as only 5-8% of patients with psoriasis develop psoriatic arthropathy.

What are the patterns of joint involvement in psoriatic arthropathy?

- **Asymmetrical oligoarthritis**, involving mainly the **DIP joints**:
    - Occurs in **25% of cases**, although most patients progress to a polyarticular arthritis with time
    - Usually affects the hands and feet first, and may cause inflammation of both the flexor tendon and synovium leading to the 'sausage' appearance of Dactylitis
- **Symmetrical polyarthritis**, involving the PIP and MCP joints with sparing of DIP joints, i.e. **rheumatoid pattern**:
    - The most common form, occurs in **60-80%** of cases
    - This can be clinically indistinguishable from RA
    - **rheumatoid factor** and **anti-CCP antibodies** are typically **absent**
    - Other differentiating features from RA are absence of subcutaneous nodules, and some degree of **asymmetry**

- Can affect hands, wrists, feet, and ankles

- **DIP arthritis**
  - Although considered a classical presentation of psoriatic arthropathy, this form only affects **5- 10% of patients**, **mostly males**
  - Associated **nail involvement** and nail bed swelling (**paronychia**) may make appreciation of distal joint arthritis difficult
- **Arthritis mutilans**
  - **Aggressive**, deforming arthritis, affecting **1- 5%** of patients
  - **Resorption of bone** with dissolution of joint leads to **'telescoping** of digits within redundant overlying skin.
- **Spondylitis +/- sacroiliitis**
  - This occurs in **20-40% of patients**, **mostly males**
  - Spondylitis may occur with or without sacroiliitis.
  - Vertebral involvement is **asymmetrical** (symmetrical in ankylosing spondylitis)

Aside from the skin lesions, which features distinguish rheumatoid arthritis from psoriatic arthropathy?

Rheumatoid arthritis

- More common in women
- Sparing of distal joints
- Symmetrical
- Tenderness precedes deformity
- No enthesopathy
- X-Ray: Periarticular swelling, joint erosions, juxtaarticular osteoporosis, and uniform joint space- narrowing
- **Rheumatoid factor in 70%**
- **Anti-CCP antibodies in 60%**
- Rheumatoid nodules in seropositive disease
- Weak association with **HLA-DR4 and TNF-a polymorphisms**

Psoriatic arthropathy

- Equal sex distribution
- **Distal joints** commonly involved
- **Asymmetry**, even in polyarthritis
- **Less tender**, so may present with **deformity**
- **Enthesitis**, **spinal** involvement and **dactylitis** may occur
- Early deformity, with bone lysis and telescoping of digits, causing the 'pencil in cup' appearance
- **Rheumatoid factor in 10%**
- **Anti-CCP antibodies in 15%**
- Rheumatoid nodules typically absent
- Strong association of psoriatic spondylitis with **HLA-827**

Notes:

- **Psoriatic arthritis** (PsA) develops in **5–10 %** of patients with psoriasis, **more commonly** in those patients **with nail involvement**.
- **Axial arthritis** accounts for **only 2 %** of cases of psoriatic arthritis.
- 70 % of patients have skin psoriasis for > 10 years before the development of PsA.
- In the remaining 30 % of patients the arthritis precedes or coincides with the onset of skin psoriasis.
- The **sex distribution is equal**, except for the inflammatory **spondyloarthropathy**, where there is a **3-fold increased male** predominance.
- The **typical age** of onset is between **35–50 years** old.
- Having a **first degree relative** with PsA increases one's chance of developing the condition **50-fold**, and a **father** with the disease **confers twice the risk** as a mother with the disease to a child.

Guttate Psoriasis (Small Numerous Plaques, **Tear Drop Like**)

- Preceded by **Strept Infection**

- Remember, that psoriatic arthropathy can occur with minimal skin involvement.
- In **20% of cases**, the **arthropathy precedes the onset of psoriasis**, in some cases **by up to 20 years**.

- *There is no evidence of a link between the activity of the skin lesions and the arthropathy.

- **The joint distribution:**
  - **Smaller joints** e.g. hands and feet.
  - **Larger joints** e.g. shoulders, elbows, knees. Enquire about the **number involved**. **Oligoarthritis** effects **1–4 joints** and, in psoriatic arthritis, is often associated with massive effusions.

Psoriatic arthropathy can occur with minimal skin involvement.

- In 20% of cases, the arthropathy precedes the onset of psoriasis, In some cases by up to 20 years.
- Similarly, psoriasis may be present without evidence of arthropathy, as only 5-8% of patients with psoriasis develop psoriatic arthropathy.

Figure I5.49 (a) Psoriasis and arthritis mutilans. Note the telescoping of the thumbs and the fingers on the right. (b) Nail pitting.
(c) Distal interphalangeal arthropathy and nail changes. (d) Onycholysis.
(e) Advanced nail changes (note the psoriatic plaques
and hyperkeratosis of the nail beds). (f) Note the typical plaque on the forearm and telescopic middle finger. (Continued)

Figure I5.49 (Continued) g,h - Indistinguishable from rheumatoid arthritis. Note plaques in (g) and nails in (h).

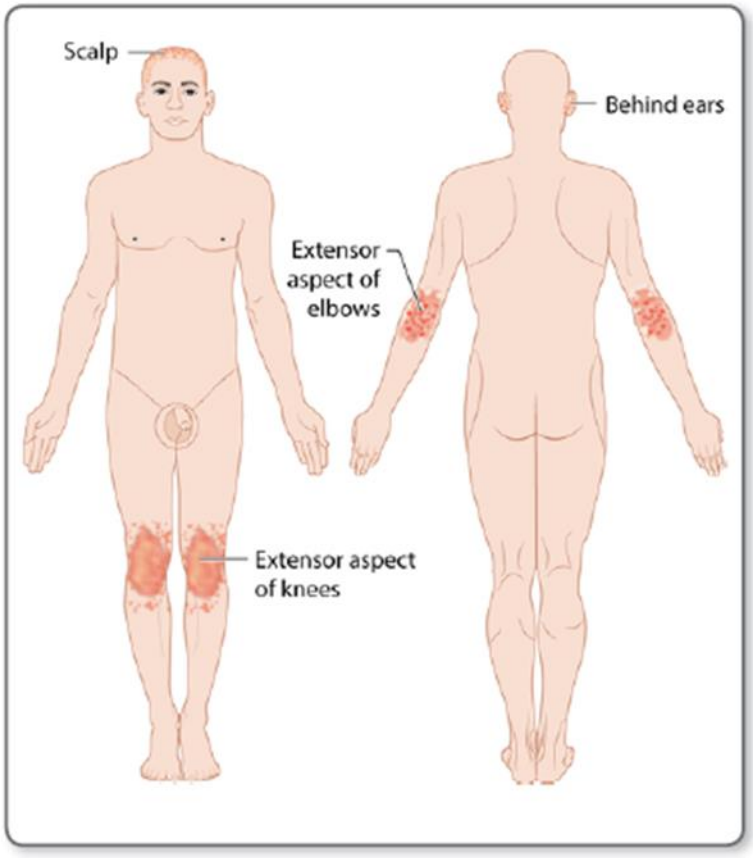

Figure 5.2 Sites of plaques in psoriasis. The main sites of plaque found in chronic plauque psoriasis, namely the extensor aspects of the elbows and knees, the scalp and behind the ears.

Fig. 129.1 Psoriatic arthritis, with asymmetric arthritis pattern. (With permission from Habif 2009.)

Fig. 129.2 Arthritis mutilans with destructive changes, joint deformity of the hand and pancompartmental ankylosis of the wrist. (With permission from Firestein et al. 2008.)

MRCP-PACES

Brief Clinical Consultation

Purpura

You are the doctor in the clinic today
This Mrs. Suzy, 45 years old is having skin rash in her limbs

Confirmations:

- Self
- Patient
- Agenda

Opening question:

- You got troubled with skin rash in your limbs
- Could you tell me more about that?
- Yes doctor, for 1 week I got this skin rash in my arms and legs

Empathy and sympathy:

Analysis of skin rash:

ODPARA

- **Onset**
  - When did it start, Sudden or gradual?
- **Duration**
  - For how long it is there?
- **Progression**
  - Is it the same, increasing or decreasing?
- **Association**
  - Any other symptoms you have?
  - Like what?
  - Joint pain?
  - Headache?
- **Relieving factors**
- **Worsening factors**

- Is it painful?
- Is it oozing?
- Is it itching?
- **Is it blancheable**, I mean fades on pressure?
- What the color of the rash?
- Is it related to sun exposure?
- You said it is in limbs, any other site involved?
- Any bleeding anywhere in your body?
- Any frothy urine – **amyloid - uremia**?
- What about the color of your urine?
- Any high body temperature?
- Any contact with sick patient- **meningococcal meningitis**?
- What about your diet, is it balanced- **vitamin C**?

- Any yellow discoloration of white of your eyes - **CLD**?
- **Any loose motion- HUS?**
- **Can I see it**
    - Red brown colored macular lesions over the hands and upper limbs.

Drug history:

- Any allergies?
- Show me your medication list

Past medical History:

- Any medical condition I should be aware of?
- **I have rheumatoid arthritis**

Family History:

- Similar conditions
- Chronic illnesses

Social history:

- What is your job?
- QOL
- May I ask a private question?
- What about your period?
- Alcohol
- Smoking

Can I examine you?

- Purpura in both upper and lower limbs
- They do not blanch under pressure.
- No varicose veins
- Joints:
    - Symmetrical deforming arthropathy of the small joints of the hands mainly involving the MCP and PIP joints
    - Subcutaneous nodules over the extensor surfaces of the upper limb
- No organomegaly

What is your concern?

- **What is wrong with me?**
- From what you told me and after examining you, most likely you have a condition called Purpura
- The term purpura is usually used to refer to a **skin rash in** which **small spots of blood appear on the skin.**
- A purpuric rash is **not a disease,** but it is caused by conditions that **result in blood leaking into the skin** and other body surfaces
- Most likely it is caused by medicine that you are taking to your rheumatoid arthritis
- We need to do some blood tests and imaging to confirm our diagnosis and will refer you to joint doctor to adjust your medications
- If results came with low blood count, then you will need admission to observe you and to receive further treatment and will be explained well to you thence
- Is that okay with you?

What is your diagnosis?

- Purpura most likely drug induced - treatment of underlying rheumatoid arthritis - steroid or gold therapy

What is your differential diagnosis?

1. Platelet defect
2. Capillary defect
3. Coagulation defect

How would you investigate a patient with purpura?

- Often the cause of purpura may be clear, i.e. steroid therapy.
- If the cause is not clear, then the following investigations can be requested (some wilt be dependent on clinical suspicion):
    - Full blood count (FBC)
    - Blood film
    - Clotting profile
    - Fibrin degradation products
    - Autoimmune profile
    - Serum protein electrophoresis
    - Bone marrow biopsy
    - Skin biopsy

Questions commonly asked by examiners

What are the causes of purpura?

Platelet defect

- **Thrombocytopenia**
    - Drugs
    - DIC
    - Bone marrow replacement (malignancy and myeloproliferative disorders)
    - Hypersplenism
    - ITP
    - TTP, HUS
    - Aplastic anemia.
- **Uremia**
- **Chronic liver disease**
- Insecticides

Capillary defect

- Age
- Corticosteroids (endogenous or exogenous)
- **Drugs**
- **Vasculitis**
    - Henoch Schonlein Purpura
    - polyarteritis nodosa
    - Churg-Strauss syndrome
    - Wegner's granulomatosis
    - SLE
    - Infective endocarditis
    - Sjogren's syndrome
    - Cryogtobulinaemia
    - Waldenstrom's macroglobulinaemia.
- **Cholesterol embolism**

- Ehlers-Danlos syndrome
- Pseudoxanthoma elasticum
- **Hereditary hemorrhagic telangiectasia**
- **Scurvy**
- **Amyloidosis**
- **Venous stasis**

Coagulation defect

- **Antithrombotic therapy**
    - Aspirin
    - Warfarin
    - heparin
- **Von-Willebrand's disease**
- **Haemophilia**
- **DIC**
- **Amyloidosis**
    - capillary fragility
    - factor X deficiency

Clinical notes

- Purpura is caused by bleeding from capillaries into the skin.
- These lesions are painless and non-blanching and can be palpable or non-palpable.
- Purpuric lesions include petechiae and ecchymoses.
- (a) Petechiae: round pin-point lesions, 1-3 mm in diameter often red brown in color and usually develop on dependent portions of the body
- (b) Ecchymoses are larger than petechiae, and often present as red-purple blue or yellow-green bruises and can arise anywhere on the body because of trauma

- The cause may be evident on general examination (as in the above case).
- If unable to find a cause for the purpura, then it is best to give a diagnosis of purpura, and provide a list of differential diagnoses

MRCP-PACES

Brief clinical consultation

Restless leg syndrome

Scenarios:

You are SHO in clinic
Mr. Edwardo is 41 years, complaining of **abnormal sensation in legs**

Other scenarios:

- **Abnormal leg movement**
- **Abnormal sensation:** tingling, burning, itching, or throbbing
- a "creepy-crawly" feeling like **fizzy water** is inside the blood vessels in the legs a **painful cramping sensation** in the legs, particularly in the calves

Opening question:

- you got troubled with abnormal sensation in legs
- Could you tell me more about that?

Analysis of the complaint:

ODPARA - OCD

- When did it start?
- Is it sudden or gradual?
- Is it first time?
- How often it is coming?
- Is it increasing or decreasing?
- What increases it?
- Is it increasing by rest or when you move your leg?
- Did anyone notice abnormal limb movement during sleep?
    - Periodic limb movements in sleep (PLMS)
- Is it affecting your sleep

- **How unpleasant these symptoms are**
- Is it increasing in any specific time of the day?
- **Is it more at night?**
- Anyone notice abnormal limb movement while you are sleeping?
- Any crawling sensation in limb?

Differential diagnoses analysis:

1. **Familial**
    - Anyone affected in the family?
2. **Idiopathic - primary**
3. **Underlying medical conditions**
    - **DM**
    - **Uremia - water work**
    - **IDA** - tiredness, pale
    - **Parkinson's** disease
    - Fibromyalgia
    - RA
    - **Hypothyroidism**
4. **Pregnancy**

Can I examine you?

- Pallor
- Thyroid
- Blood sugar markings in finger bulbs
- **CNS**
    - Power
    - Sensation
- Check urine
- Check blood sugar

PMH:

- Any PHM I should be aware of?!
- Any DM

DH:

- Show me your medication list

Social:

- How much these symptoms affect your daily activity?
- Private question
- What about your **period**
- Is it heavy
- Any possibility you are **pregnant**?
- Driving?
- Are these symptoms affects your driving
- Smoking
- Alcohol

What is your concern?

What is wrong with me doctor?

- From what you told me and after examining you most likely you have a condition called RLS
- It is a medical term for a medical condition in which there is problem of the nervous system that causes an **overwhelming irresistible urge to move the legs**.
- What we need to do is to arrange some blood tests to confirm our diagnosis and to rule others
- **Mild restless legs syndrome** that is not linked to an underlying health condition can be managed with just a **few lifestyle changes**.

What causes it doctor?

- In most cases, there is no obvious cause of restless legs syndrome.
- This is known as **idiopathic or primary restless legs syndrome**, and it can run in families.
- It might be linked to a protein dopamine secreted by part of your brain and it controls movement in the body
- This substance **falls during end of the day**
- In some cases, restless legs syndrome is caused by an underlying health condition, such as iron deficiency anemia or kidney failure.
- This is known as **secondary restless legs syndrome**.

Is it related to my pregnancy?

- There is also a link between restless legs syndrome and pregnancy.

- **About 1 in 5 pregnant women** will experience symptoms in the last 3 months of their pregnancy, although it is not clear exactly why this is.
- In such cases, restless legs syndrome **usually disappears** after the woman has given birth.

Examiners questions:

What are your findings?

- Only pallor

How to investigate:

- **No single diagnostic test**
- **Underlying conditions**
  - DM
  - IDA
  - RFT
- **Sleep tests**

Management:

- **Non- pharmacological:**
  - **Good sleep habits**
  - **Avoid triggers**
    - Lack of exercises
    - Smoking
    - Alcohol
    - Avoid caffeine at night
  - **During an episode of restless legs syndrome, the following measures may help relieve your symptoms:**

    - **Massaging** your legs
      Taking a **hot bath** in the evening
    - Applying a **hot or cold compress** to your leg muscles
    - Doing activities that **distract your mind**, such as reading or watching television
    - **Relaxation exercises**, such as yoga
    - **Walking** and **stretching**
- **Pharmacological:**
  - **Underlying cause**

- **If symptoms are severe**
  - **Aiding sleep:**
    - **Benzodiazepines**
    - **Dopamine agonists:**
      - ✓ ropinirole
      - ✓ pramipexole
      - ✓ rotigotine skin patch
  - **Painkillers**
    - **A mild opiate-based painkiller**, such as **codeine**, may be prescribed to relieve pain associated with restless legs syndrome.
    - **Gabapentin** and **pregabalin** are also sometimes prescribed to help relieve painful symptoms of restless legs syndrome.

- **Any medications that might trigger RLS?**
  - some antidepressants
  - antipsychotics
  - lithium
  - calcium channel blockers
  - some antihistamines
  - metoclopramide

- **Any risk for having RLS?**
  - Recent research found people with restless legs syndrome may be more likely to develop **cardiovascular disease**, such as coronary heart disease or stroke, compared with people who do not have the syndrome.

MRCP-PACES

Brief clinical consultation

Stroke in young patient

Scenario:

- You are a doctor in the clinic
- Mr. Edwardo is 21 years with sudden left sided weakness

Confirmation:

- Self
- Patient
- Agenda

Opening question:

- You got troubled with left sided weakness
- Could you tell me more about that

Analysis of the complaint:

ODPARA-OCD

- **Onset** - sudden or gradual?
  - **Duration, Progression, Recovery:**
    - TIA < 24 hours
    - Stroke > 24 hours
    - Multiple sclerosis, there will be periods of recovery
- For **how long** the weakness
- **When** did it start?
- **Where** is the weakness exactly?
- Any weakness *anywhere else*?
- Difficulty in walking
- Is it the same, progressing or improving?
- What the **nature** of weakness? Is it **flobby** or **stiff**?

Screen for other CNS symptoms:

- Any headache

- Any dizziness
- Any blurring of vision
- Any loss of consciousness
- Any difficulty in speech
- Any fits
- Any loss of control of water work or back-passages
- Any altered sensation

Screen the differential diagnosis:

CNS:

1. **Stroke**
2. **Subarachnoid Hemorrhage**
    - **Berry aneurysm** – SAH, Arterial dissection - ADPKD – change in water work tummy pain, family history
    - **AVM** – HHT, skin rash, nosebleed
3. **Migraine**
    - **Hemiplegic Migraine**
        - Transient weakness which improves and follows by headache
        - Migraine aura
        - Improves by calm environment
        - Increase by exposure to light
4. **Epilepsy**
    - **Todd's paralysis**
        - Aura
        - Flashes of light
        - Abnormal smelling
        - Epigastric sensation
5. **Space occupying lesion**
    - Headache worsening with bending, sneezing, or coughing
    - Vision problem
    - Getting sick or feeling sick

Hematological:

- **PCV**
- **Sickle cell disease:**
    - Looks pallor than usual
    - Yellow discoloration of whites of eyes

        - Dark urine
        - Joint pain
- **Others:** protein C, protein S, antithrombin III deficiency, factor V Leiden, PNH

Hyperlipidemia:

- Any history of high cholesterol?
- HTN
- DM

Cardiac:

1. Mitral stenosis - AF
2. PFO
3. VSD
4. ASD
5. MVP
    - Any heart racing
    - Chest pain
    - Any heart problem before problem before
    - High body temperature - IEC

Vasculitis:

- Fever, joint pain, rash
- **Behcet's disease**
    - Soreness in mouth and private area
    - Eye redness
    - Headache - cavernous sinus thrombosis
    - Lung symptoms - PE
    - Limb symptoms – DVT

Carotid dissection – neck pain

Homocystinuria

Syphilis

Trauma

APL

- may I ask a private question – if female – what about your period
- Any chance of pregnancy, any loss of pregnancy

SLE

Drugs history:

- **Illicit drugs** - Cocaine, amphetamine
- OCP – ask women doctor to prescribe safe alternative

Family History:

- Weakness or stroke in young
- **Hyperlipidemia**

Social history:

- Job
- QOL
- Smoking
- Alcohol
- Advise you to stop driving

Can I examine you:

- **Pulse** - AF
- Carotid bruit
- **CVS:**
    - Apex - mid diastolic rumbling murmur in mitral area - MS
- **CNS:**
    - Tone
    - Power
    - Sensation
    - Cerebellar signs

What is your concern?

What is wrong with me doctor?

- After what you told me and after examining you most likely you have stroke
  Due to .....
- **We need to admit you**
- To refer you to group of specialists including nerve doctor, physiotherapist, occupational therapist
- If sickle cell disease, then blood doctor

Is it stroke?

- Unfortunately, stroke is one of the possibilities, that's why we need to do exclude it by doing some tests and imaging

Examiners' questions:

Present your finding:

- This young patient with signs of UMN in form of
    - Positive pronator drift
    - Pyramidal weakness with extensors and distal muscles weaker than flexors and proximal muscle groups
    - Hypertonia
    - Hyperreflexia
    - Irregular pulse being in AF at rate of 77 beats/minute

What are your differential diagnoses of the cause f weakness in this patient?

1. Mitral Stenosis with AF
2. APL syndrome
3. Sickle cell disease
4. Hyperlipidemia
5. Multiple sclerosis
6. Hemiplegic migraine

What are your differential diagnoses of transient weakness in this patient?

1. Multiple sclerosis
2. TIA
3. Hemiplegic migraine

What are the differential diagnoses of weakness cause in this patient?

1. Stroke
2. Trauma
3. Tumor

How you will investigate this patient?

- **Basics:**
    - CBC - PCV
    - **Inflammatory markers**
        - ESR- PCV
    - **Lipid profile**

- **Coagulation screen**
  - Protein S, C, antithrombin III
- **CXR**
- **ECG** - AF
- **Echo** - PFO, VSD, MS
- **Carotid** arteries doppler US
- **Collagen vascular disease:**
  - ANA
  - Anti dsDNA
  - Anti-phospholipid
  - Anticardiolipin
  - Urinary homocysteine
- **Syphilis screening**- TPHA, VDRL
- **CT/ MRI brain**

How to manage this case?

- **Non-pharmacogical**
  - Education
  - Counseling
  - **MDT**
  - **Modify the risk factor - DM, Obesity**
  - Stop smoking and alcohol
  - Lifestyle modification - Exercise, diet
- **Pharmacological:**
  - Anti-platelets - aspirin
  - Statins - to all patients
  - Treat AF
  - Treat the primary cause

How you stratify risk of stroke in TIA?

ABCD2 Score:

- **Age > 60** - 1
- **BP > 140/90** - 1
- **Clinical:**
  - ✓ Speech no weakness 1
  - ✓ Weakness 2

- **Duration**
  - **< 1 hour 1**
  - **> 1 hour 2**
- **DM 1**
- **Score:**
  - 1-3 mild
  - 4-5 moderate
  - 6-7 high risk

What are the causes of recurrent weakness?

- **CV diseases:**
  - MS
  - AF
- **Hematological:**
  - Hyperviscousity
  - PCV
  - Protein C, S, AT III deficiency
- **CNS diseases:**
  - Hemiplegic migraine
  - Epilepsy - Todd's palsy
- **Rheumatological:**
  - Wegner's granulomatosis
  - Takayasu
  - PAN
  - APL
- **Others:**
  - Hysteric hemiplegia
  - HTN
  - AVM
  - Homocystinuria
  - Amyloidosis

What are the DVLA rules in stroke and TIA?

Group 1 entitlement ODL – car, motorcycle

- **Stroke:**
  - Must not drive for 1 month

    - May resume driving after this period if the clinical recovery is satisfactory.
    - There is **no need to notify DVLA unless there is residual** neurological **deficit** 1 month after the episode; in particular, visual field defects, cognitive defects, and impaired limb function.
    - Minor limb weakness alone will not require notification unless restriction to certain types of vehicle or vehicles with adapted controls is needed.
    - Adaptations may be able to overcome severe physical impairment
    - Seizures occurring at the time of a stroke/TIA or in the ensuing 24 hours may be treated as provoked for licensing purposes in the absence of any previous seizure history or previous cerebral pathology.
- **TIAs:**
    - Must not drive for 1 month.
    - Single TIA no need to notify DVLA.
    - Multiple TIAs over a short period will require 3 months free from further attacks before resuming driving and DVLA should be notified

Group 2 entitlement VOC – LGV/PCV (lorry/bus)

- License refused or revoked if condition sudden and disabling.
- Consider underlying diagnosis and if likely to cause recurrent attacks, must be symptom-free and completely controlled for 1 year from last attack before re-application.
- License refused or revoked for 1 year following a stroke or TIA, Can be considered for licensing after this period provided that there is no debarring residual impairment likely to affect safe driving and there are no other significant risk factors.
- Licensing may be subject to satisfactory medical report including exercise ECG testing.
- Where there is imaging evidence of less than 50% carotid artery stenosis and no previous history of cardiovascular disease Group 2 licensing may be allowed without the need for functional cardiac assessment.

- However, if there are recurrent TIAs or strokes, functional cardiac testing will still be required.

MRCP-PACES

Brief Clinical Consultation

Takayasu Arteritis

You are SHO in the clinic
Mr. Mary, 42 years, complains of headache for 9 weeks
Please assess and advise

Confirmations:

- Self
- Patient
- Agenda: I have letter from your GP mentioning that you have been complaining of **recurrent headache** for last 9 weeks

Checks:

- Understanding
- Expectations
- I am going to take some notes during conversation, and it will be confidential, and I will give you my full attention

Back-ground:

- You had been troubled with **recurrent headache** for last 9 weeks
- **Could you tell me more about it?**

Analysis of complain:

ODPARA

Headache:

- Onset- course, duration, progression, worsening and improving factors, associated symptoms
    - **When did it start** exactly?
    - **Where** in your head exactly, temples or all-over?
    - Is it **sudden** or **gradual**?
    - Is it **decreasing** or **increasing** or the same?
    - Is it coming **on and off** or **continuously**?
    - **Anything worsening** it – like sneezing, straining, bending forward, cough, strong voices, flashes of light, alcohol?
    - **Anything improving** it like rest, calming down, and darkness?

- For **how long** it goes
- **Timing**: any diurnal variation? Is it more in morning or night?
- **Frequency**: how many times per week
- For **how long** attacks persisted
- What is the **nature** of the headache- compressing, throbbing band like, pulsatile, dull aching?
- **Intensity**: what is the **grade** of pain, from 0 to 10
- **Radiation**: is it radiating anywhere like to the nape, eyes
- **Aura**: any preceding symptoms like heart burn, feeling sick, strange voices or visual hallucination

Systemic review:

- **Constitutional symptoms**
  - Pain in multiple joints
  - Weakness of upper limbs
  - Loss of weight
  - Malaise
  - **High body temperature** - low grade, no chill, rigor, or sweating.
- **joint pain**
  - Mild to moderate
  - Multiple joints including small joints of hands, wrists, elbows, knees, and ankles
  - No swelling of the joints or morning stiffness.
- The patient also complains of loss of appetite and substantial weight loss
- Jaw pain
- Chest pain – MI, pericarditis, pulmonary HTN
- Muscle pain
- Pain in hands
  - Pain in both upper limbs
  - Appears after 10 to 15 minutes of manual work
  - Subsides after taking rest.
  - **Raynaud's** phenomenon
- Pain in legs- **Claudication**
- **CNS:**
  - Fit
  - Visual disturbance
  - **Weakness** of both upper limbs.

Past medical history:

- **HTN - Renal artery stenosis**
- Heart failure
- Stroke
- Mini stroke

Past surgical history:

FH:

Drug history:

Social history:

- Job
- QOL
- Support needed
- Smoking
- Pregnancy
- Driving

Physical examination:

- Mildly anemic
- **Fundoscopy**
  - Hypertensive changes
- **Neck:**
  - **Carotid bruit -** Bruit is present over both carotids
  - **Subclavian bruit**
  - **Scars for previous surgery**
- **Peripheral pulses:**
  - Decreased pulsation in brachial arteries (one or both arm)
- **Blood pressure:**
  - Difference of at least 10 mmHg of systolic BP between arms
- **Abdomen:**
  - **Renal bruit**
- **CVS:**
  - HTN
  - CCF
  - **AR -** There is a high pitched, blowing, early diastolic murmur best heard in the left lower parasternal area, with patient bending forward and breathing hold after expiration.
  - Pericarditis
  - Raynaud's phenomenon
  - pulmonary HTN
- **CNS:**
  - Power
  - Sensation
- **Upper limbs:**
  - Pulse - All peripheral pulse in upper limbs are absent.

- Peripheral pulse: All peripheral pulse in upper limbs are absent. In the lower limbs, pulse is present,
- 88/min, regular.
- Raynaud's phenomenon
- Small joints of hands, wrists and elbows are mildly tender

- **Lower limbs**
  - Pulses - pulse is present, 88/min, regular.
  - Ischemic changes
- BP: Not recordable in upper limbs. (It should be recorded in the lower limb with 18 cm cuff).

Addressing concerns:

- Your symptoms may be related to a condition called Takayasu Arteritis
- It is due to soreness of the large blood channel and mainly affecting the aorta which is the main blood channel carrying blood from heart to rest of the body
- This leading to narrowing of the blood channel and hence when the organs do not get the sufficient blood supply, symptoms occur
- We need to arrange some blood tests and scan the blood channels
- Treatment is controlling your blood pressure and controlling the soreness initially with medications

Examiners' questions:

What is your diagnosis?

- **Takayasu arteritis**

Why Takayasu's disease?

- Because all the pulses in the upper limbs are absent and there is carotid bruit.

What are the differential diagnoses?

1. Temporal arteritis / GCA
2. Takayasu arteritis
3. Atherosclerosis

How you will investigate this case?

- **Basic investigations**
  - CBC
    - Normocytic anemia
  - **Inflammatory markers**
    - ESR, CRP may be high
  - **RFT**
  - Serum immunoglobulin is high.
  - **Urine analysis to see renal involvement-HTN**
- **CT angiography or MRA** to see stenosis or aneurysms

- **Aortography** of aortic arch and its branches, **renal angiogram** shows narrowing, coarctation and aneurismal dilatation
- **Carotid Doppler US**
- Tissue biopsy-little role
- **Echocardiogram**
- **Chest X-ray**
  - Cardiomegaly
  - widening of aorta
- **PET scanning**

How you will treat this case?

- **Controlling hypertension**
- **Treating CVS risk factors**
- **Controlling inflammatory process:**
  - **High dose corticosteroid**
    - **Prednisolone** 40 to 60 mg daily or 1 to 2 mg/kg.
  - **Cytotoxic**
    - If refractory to steroid or difficult to taper steroid
      1. Azathioprine
      2. Methotrexate up to 25 mg weekly.
      3. Cyclophosphamide
  - **Biological agents**
      1. **Rituximab**
      2. **Infliximab**
  - **Low dose aspirin**
- **Surgical:**
  - Reconstructive vascular surgery in selected case
      1. Angioplasty
      2. Stenting
      3. CABG

What is the prognosis?

- **Generally good**
- **Prognosis—with appropriate treatment, 5-year survival is 83%**
- **May follow relapsing and remitting course**
  1. 25% unaffected by the disease (self-limiting)
  2. 25% can perform normal daily activity in remission
  3. 50% are unable to consistently perform normal daily activities
  4. 25% will not able to do their work

What are the causes of absent radial pulse? Or unequal radial pulse?

- **Anatomical** aberration (may be **congenital**).
- **Atherosclerosis**.
- **Coarctation** of the aorta (before origin of the left subclavian artery).

- **Takayasu's** arteritis.
- **Iatrogenic**—blalock taussig shunt (done in TOF), AV fistula for hemodialysis.
- Occlusion by **thrombosis**.
- Occlusion of the subclavian artery by cervical rib or **neoplasm**.
- **Dissecting** aneurysm.

What is Takayasu's disease (pulseless disease or aortic arch syndrome)?

- It is a chronic inflammatory, granulomatous panarteritis of unknown cause involving the elastic arteries.
- It commonly involves aorta and its major branches, carotid, ulnar, brachial, radial, and axillary.
- Occasionally, may involve pulmonary artery, rarely abdominal aorta, renal artery resulting in obstruction.
- Age of onset is 25 to 30 years.
- Common in female, F:M ratio is 8:1.

What are the pathological changes in Takayasu's diseases?

- Panarteritis, with inflammatory mononuclear cell infiltration with occasional giant cell.
- There is intimal proliferation and fibrosis, scaring and vascularization of media and disruption and degeneration of the elastic lamina.
- Narrowing of the lumen occurs with or without thrombosis.

What are the types of Takayasu's disease?

- **4 types:**
    - Type 1 – localized to the aorta and its branches.
    - Type 2 – localized to descending thoracic and abdominal aorta.
    - Type 3 – combined features of type 1 and 2.
    - Type 4 – involves the pulmonary artery.

What are the clinical features?

- Common in adolescent girls and young women (F:M = 8:1), 25 to 30 years, more in Asians.
- Clinical features are:
    - General symptoms are—fever, malaise, weight loss, arthralgia, myalgia, dizziness, giddiness, headache, syncope, seizure, claudication in the upper limb.
    - There may be **aortic regurgitation**, renal artery stenosis or **anginal pain**.
    - Hypertension in 32 to 93%.
    - There may be pericarditis, myocardial infarction, congestive cardiac failure, etc.

What are the ophthalmologic findings?

- Ophthalmologic examination may show retinal ischemia, retinal hemorrhages, cotton-wool exudates, venous dilatation, and beading, microaneurysms of

peripheral retina, optic atrophy, vitreous hemorrhage and classic, wreath like peripapillary arteriovenous anastomoses.

What is reverse coarctation?

- When **pulse is absent in upper limb**, but **present in lower limb**, it is called reverse coarctation.
- It occurs **in Takayasu's disease.**

What are the causes of coarctation?

- **Congenital** (the most common).
- Rarely, may be acquired in **trauma**, **Takayasu's** disease

Takayasu's disease

- This is an arteritis which affects chiefly, but not exclusively, young women from Japan and the Far East.
- It involves mainly the **aortic arch** and the **large brachiocephalic arteries**.
- Mononuclear cell infiltrates and fibrous proliferation produce **progressive narrowing of the lumen** and reduced flow in the upper extremities and to the **brain**.
- It develops slowly so that although the **pulses gradually vanish** (hence the alternative name – **pulseless disease**), **collateral** circulation opens, allowing it to remain unnoticed for some time.
- Eventually the patient presents with symptoms such as **fainting** on **turning the head suddenly** or **rising from supine to sitting**, **atrophy of the face**, **headaches**, **cataracts**, **optic atrophy**, **weakness** and **paresthesia** of the upper extremities, **hemiplegia,** and **convulsions**

ACR diagnostic criteria

(3 of 6 are necessary):

1- Onset of disease 40 years of age or below
2- Claudication of an extremity
3- Reduced brachial artery pulsation
4- Difference in Systolic pressure of more than 10mmhg in arms
5- Aortic or subclavian artery bruit
6- Angiographic abnormality

Anecdote

60-year man with weakness and pain in left hand
Worried if it could be TIA.
I did not have a clue till I started examining.
I felt pulse in both hands and noted absent radial pulse in left hand.
Went up and absent brachial as well.
Told DD as Takayasu's and examiner frowned and asked what else.
Said subclavian steal syndrome and he gave me the thumbs up. 28/28

MRCP-PACES

Brief Clinical Consultation

Essential Tremor

You are the **SHO in the neurology clinic**.
A **48-year-old man** has been referred by his GP **complaining of handshakes** and difficulty in writing
Please assess him and inform him of your management plan.

Opening Question:

- I received a letter from your GP mentioning that you are troubled with handshakes
- Could you tell me more about that?
- **I have a tremor in both hands.**
- **It has been there for probably 5–6 years and has not changed a great deal over the past couple of years.**
- **I have not tried any medicines, but the tremor settles after a few drinks (beer).**
- **The reason I went to my doctor is that my friends had noticed a new tremor affecting my head over the past 6 months or so and mentioned it to me, and I saw a program on TV about Parkinson's disease.**
- **I am walking OK and no differently from before.**
- **My speech and writing are also pretty much the same as before.**
- **No change in bowel habit or swallowing. It gets worse when I am anxious or when giving a talk at the local Neighborhood Watch meeting that I chair every month.**

Analysis of Handshakes

ODPARA:

- **For How Long?**
- **Which limb** affected
- **Which part** affected?
- Is it unilateral or bilateral?
- Has it occurred suddenly or gradually?
- Is it getting better or worse?
- **Voice** affection
- **Head** involvement – **titubation**

- **Exacerbating and relieving factors**
    - **Exacerbants:**
        - Emotion
        - Being watched
        - Stress/anxiety
        - Exercise
        - Fatigue
        - Alcohol
    - **Relieving factors:**
        - Essential tremor often eased by alcohol
- **Effect on handwriting - bad in ET - Writing like scrawl**
- **Effect on hand functions**
- is it noticed by you, or if it has been mentioned by a relative/carer?
    - A patient with an essential tremor or cerebellar dysfunction may be more likely to notice their tremor than a Parkinsonian patient.
- **Is it at rest or when you move your hands?**
    - During change in posture **- postural tremor**
    - During movement or **approaching** a target - **kinetic tremor**
    - All the time - drugs, metabolic, physiologic
    - **Rest** - resting - Static in **Parkinson's**
    - **Intentional** tremors in **cerebellar** disease.
    - **Familial** worse on **outstretched** arms (**postural**)
- **Is it fine or coarse?**
    - Fine means the tremors are not involving a joint.
        - Parkinson's
        - Familial
        - Lithium Toxicity
        - Salbutamol Use.
        - Anxiety.
    - **Coarse means it is involving a joint**
        - Flapping Tremors.
        - Cerebellar Tremors.
- Any **Associated Symptoms**?
- **Sensory motor deficits**
- **Cerebellar signs**- any imbalances, unsteadiness, uncoordinated movement

- Confusion or **hallucination** - Lewy body dementia
- **What about your mood?**
- **Alarm:**
    - Parkinson's signs
- **Risk factors:**
- **Drugs- recreational**
- **Change in regular medicines**
- **Thyroid disease**
- **FH**

Differential diagnoses of Handshakes

- **Thyrotoxicosis**
- **Parkinson's Disease**
    - Unilateral tremor
    - Rigidity
    - Bradykinesia
    - Micrographia
    - Slurring of speech
- **Familial / Senile / Postural.**
- **Lithium** (Bipolar Disorder)
- **Cerebellar Disease** (Alcohol, Ataxia Telangiectasia, MS)
    - **Action tremor**
    - Not coordinated movements
- **Anxiety disorder**
    - Panic attack, SOB, paresthesia
    - Alcohol to suppress it
    - TTT: CBT, benzodiazepines
- **Alcohol and drug withdrawal tremor**
    - ☆ Alcohol withdrawal causes rest tremor
    - **Alcohol withdrawal:**
        - History of **alcoholism**
        - **Fine tremor**
        - Alcohol can induce **withdrawal tremor**, **liver flap** tremor and cerebellar **atrophy** related tremor
        - **All can occur together**
        - TTT: **Chlordiazepoxides** for withdrawal but not for tremor alone.
        - **Graduated alcohol reduction**

- If tremor persist with abstinence cerebellar atrophy should be excluded

- **Wilson's disease**
- **Hypoglycemia**
    - Risk factor like DM, OHGM, alcohol excess, endocrinopathy like Addison's,
    - Liver disease, Pituitary disease
    - No clinical signs but cognitive impairment during hypoglycemia
    - **Investigations**:
        - Plasma glucose, C peptide, pro-insulin,
        - Beta hydroxybutyrate
        - Screen OHGM
        - Test glucose responses to IV 1 mg glucagon - differentiate endogenous from exogenous insulin from others
        - **TTT**: glucagon self-injection im, oral Glucose
- **Flapping Tremors:**
    - Co2 Retention
    - Chronic Liver Disease
- **Other Forms of Abnormal Hand Movements:**
    - **Dystonia**
    - **Hemi-Ballismus**
- **Drugs:**
    - **B2 Agonists** (COPD, Bronchial Asthma)
        - Salbutamol
        - Theophylline
    - **Sodium valproate**
    - **Ciclosporin**
    - **Tacrolimus**
    - **Lithium toxicity tremor:**
        - ☆ Action tremor due to cerebellar dysfunction
        - Check for other cerebellar signs
        - Potentiated by use of **diuretics, dehydration**, **ACEi**, **NSAIDs**
        - Other features - nausea, vomiting, abdominal pain, diarrhea, confusion, seizures

Past Medical History

- Liver disease
- Wilson's
- Thyrotoxicosis
- Parkinson's disease
- Anxiety disorder
- Psychiatric illness
    - Bipolar disorder - antipsychotic, anti-convulsant, lithium
- CVA - basal ganglia

Drug history:

- Dose, change, duration
- Recreational – illicit drugs - cocaine, amphetamine
- **Drug withdrawal can also cause tremor**
    1. Alcohol
    2. Benzodiazepines
    3. morphine/opiates
- **Endocrine** medicines: thyroxine, steroids
- **Respiratory**: salbutamol, theophylline
- Anticonvulsants: phenytoin, valproate
- **Antiemetics**: metoclopramide
- **Antipsychotics**: haloperidol, lithium, Chlorpromazine
- **Recreational**:
- Fine tremor: beta 2 agonists, thyroxine, Steroids, theophylline, lithium, tacrolimus, ciclosporin
- Extrapyramidal sign: antipsychotic
- TTT: stop culprit drug

Toxins:

- **Organophosphates, heavy metals - Mercury**
- Tremor and other signs after **insecticides** exposure, or **herbicides** or heavy metal exposure.
- Signs: tremor, seizure, slurred speech, Anxiety
- Diagnosis: suspicious

Family History

- **ET**
- **Wilson's**
- Screen for an inherited or genetic component

- Essential tremor is called **familial tremor** if there is a family history (50% autosomal dominant pattern).
- It is usually called **benign essential tremor** if **sporadic**
- Any family history of tremor?
- Parkinson's?
- Early-onset dementia?

Social history:

- **Occupational history – mercury**
- **Impact on QOL**
    - Even in benign essential tremor, there is considerable associated morbidity, with potential for significant impairment and disability consequently.
    - It is therefore important that you assess, and are seen to assess, the functional and psychosocial effects of the tremor.
- Impact on **driving**
  Alcohol intake.
    - In **benign essential tremor**, symptoms are often **alleviated by alcohol**, with a propensity for alcohol dependence.
    - Alternatively, **alcohol** may be the underlying **cause** of any **cerebellar disease, with resultant tremor**.

Welfare:

- **Job affection**
- **Disability benefit**
- Need to **inform the DVLA**

Can I examine you?

Start by concern - Tremor

- Comment about **character of tremor**
    - coarse/fine
    - resting/kinetic/action
- Lift both arms outstretched and observe tremor
- NB: essential tremor is seen in hands and arms, when arms are outstretched and at the end of a task directed action, e.g. drinking liquid from a glass; can be unilateral or bilateral

1. Postural tremor

2. Resting tremor - Parkinson's
3. Action tremor - cerebellar

- Inspect the patient to assess for the presence of a **resting tremor**, looking specifically for a **pill-rolling Parkinsonian tremor**.
- It may be necessary to utilize **distraction to elicit** a resting tremor.
- Screen for **postural or action tremor**, often by performing a hand or **cerebellar examination**.
- **A re-emergent tremor** can often be useful in distinguishing between a subtle essential tremor and the resting tremor of Parkinson's.

- **Look at the head.**
  - **Isolated head tremor** is **not** a **feature** of **Parkinson's** disease.
  - A '**yes-yes' tremor** suggests essential tremor, a '**no-no' tremor**, especially associated with **torticollis**, suggests a **dystonic tremor**.
- **Handwriting**
- **Thyrotoxicosis**:
  - Pulse - tachycardia, AF
  - Thyroid gland
- N**eurological examination**:
  - **Parkinsonian signs**
    - Pill-rolling resting tremor
    - Occurs at rest
    - Expressionless face
    - Usually starts off as unilateral and asymmetrical.
    - Usually affects the hands but can involve lower limbs, but not the head and neck.
    - It is exacerbated by stress, infection, or anxiety
    - Improves with action any changes in gait, handwriting.
    - See old hand-writing samples
    - Any change in voice.
    - Difficulty swallowing.
    - Drooling of saliva
    - Any double vision (tremor from Parkinson's plus syndrome of supranuclear palsy)

        - Any cramps in the hands or feet, or turning of the head (dystonia)
        - Any postural dizziness, sphincter disturbance, palpitations (autonomic symptoms in Parkinson's plus syndrome, e.g. Shy–Drager syndrome)
        - Any deterioration in cognitive function (dementia)? Or hallucinations (Lewy body dementia)
        - Clasp-knife rigidity with cog-wheeling
    - **Cerebellar signs**:
        - Ataxia
        - Dysdiadochokinesia
        - Nystagmus
        - Past-pointing
        - Intention tremor
        - Slurred speech - **Staccato**
        - Hypotonia
- **No** other Red Flag **signs to suggest parkinsonism** or any **cerebellar** signs or symptoms
- **Thyroid:**
    - Goiter
    - Eye disease
- **Wilson's:**
    - Signs of CLD

What is your concern?

Is it Parkinson's disease?

- After what you told me and after examining you, most likely you have a condition called benign essential tremor causing the handshakes you have and the difficulty in writing
- I do not think it is Parkinson's disease as there are no other features.
- We would like to do some blood tests to confirm the diagnosis and exclude others
- The initial management in benign essential tremor is lifestyle modification, with avoidance of caffeinated drinks and ensuring you get good quality and duration of sleep.
- It would be good if you reduce your alcohol now as I will be giving you medication which will help with the symptoms.
- Will refer you to physiotherapist and occupational therapist
- I need you to inform DVLA about diagnosis

- Do you have any further questions or concerns I can address for you today?'

I am still thinking have Parkinson's disease

- Very unlikely.
- We will see how you respond to the β-blockers.
- You have no features of Parkinson's disease.

Will it get worse?

- Some run a benign course
- some slowly progress to become coarser or involve other parts of the body.

Do you have any treatments for it?

What is your diagnosis?

State the most likely diagnosis based on the history and clinical findings

- 'The patient history and clinical examination are consistent with a diagnosis of **benign essential tremor**.'

Differential diagnoses

1. Benign essential tremor
2. Parkinson's disease
3. Parkinson's plus
4. Cerebellar syndrome

Remember that in a **young person**, in addition to considering benign essential tremor, you should **consider Wilson's disease** if **any cerebellar disorder** is present.

How you will investigate this case?

- Although it is a clinical diagnosis, however we need to do some tests to exclude other differential diagnosis
    - Plasma glucose - hypoglycemia
    - Thyroid function test
    - liver function tests
    - B12
    - Serum copper and caeruloplasmin in younger patient (to exclude Wilson's disease)
    - Clotting tests, copper level
    - Drugs levels- tacrolimus, lithium
    - Urinalysis: urinary copper level
    - Toxicology screen

- Neuroimaging:
- CT, MRI - demyelinated disease, SOL
- MRI brain only needed if structural lesion or cerebrovascular disease in basal ganglia is suspected causing cerebellar disease
- **DAT scan** - **Parkinson's** - asymmetrical loss of presynaptic dopaminergic receptors

How you will treat this case?

- **Nonpharmacological:**
  - Physiotherapy
  - **Occupational therapy**
  - **Psychological support**
  - It is important to counsel the patient on **lifestyle adaptations**, which can help with the symptom burden.
  - For example, **limiting the intake of caffeinated drinks**, ensuring **adequate sleep levels**, and **avoiding stress**
  - If the patient has reported a significant alcohol intake, you should seek to counsel them about the dangers of using alcohol to control their tremor and, if appropriate, refer them to **community alcohol liaison services.**
  - You can also inform the patient that there is **a National Tremor Foundation** to provide help and **support** to those with tremor.
- **Pharmacological:**
  - **Beta blocker (1st line)**
    - The first-line pharmacological management of benign essential tremor is beta-blockade with propranolol.
    - Propranolol (crosses blood–brain barrier) in low dose and then titrate up
    - propranolol 40 mg 2–3 times daily
  - **Primidone (2nd line)**
    - If beta-blockade is ineffective, the anticonvulsant primidone can be used.
    - Initially 50 mg od,
  - Others include **benzodiazepines**, **calcium channel blockers**, **gabapentin**.

- **Deep brain stimulation**
  - NICE has recently released a consultation document relating to **deep brain stimulation** for essential tremor, but most candidates would correctly wish to avoid such discussions in the PACES examination.
  - Thalamotomy or thalamic deep brain stimulation can be tried in very severe and debilitating cases

Do you know any test to diagnose essential tremor?

- Mostly from tremor history, including family history, age of onset, clinical findings, and response to β-blockers.
- **Electromyography** or **tremographic accelerometer** can be used to **assess the frequency**, **amplitude**, and **rhythmicity of the tremor**.
- Severity and response to treatment can be assessed by functional assessment, **Tremor Scale** and using **Archimedes spirals** (getting patient to draw smooth spiral on a piece of paper).

Do you know of any tests to exclude PD?

- **Good history**-taking and **examination** skills are paramount.
- If suspect PD or in atypical tremor**, DaTscan** (**ioflupanel-123 injection**) can help to **differentiate** between **essential tremor** and **parkinsonian** syndrome.
- It **detects dopamine transporters** using single photon emission computed tomography (**SPECT**).
- It **measures** the amount and **location of radioactive ioflupane I-123 in the brain**.
- However, this test cannot differentiate between idiopathic Parkinson's disease and multisystem atrophy or PSP.
- The test is **normal in essential tremor**.
- The scan can be used as an adjunct to clinical examination.

Tremor is defined as an **involuntary rhythmic movement**.

Types of tremor

Resting tremor :

- Parkinson's disease

Postural tremor (worse with arms outstretched):

- **Benign essential tremor** (50% familial) improves with EtOH
- **Anxiety**
- **Thyrotoxicosis**
- **Metabolic**: CO2 and hepatic encephalopathy
- **Alcohol**

Intention tremor :

- Seen in **cerebellar disease**

MRCP-PACES

Brief Clinical Consultation

Yellow Nail Syndrome

Scenario

You are a SHO in the clinic
45 years old, Miss. Mary
Complain of lower limb swelling

This patient, presenting with shortness of breath, has been referred to the respiratory clinic for assessment .
Please examine her respiratory system and comment on your findings

Confirmations:

- Self
- Patient
- Agenda

Opening question:

- You got troubled with leg swelling
- Could you tell me more about that?

Brief analysis of leg swelling:

OCD - ODPARA:

Legs swelling:

- Onset - Sudden or gradual
- Course - Progressive, same, or regressive
- Duration – for how long you are suffering from it?
- **Association:**

  - **CVS:**
    - SOB
    - Cough
    - PND
    - Orthopnea
    - Heart racing
    - Chest pain
  - **Malignancy:**
  - **AIDS**

        - Pumps or lumps
        - High body temperature
    - **Nephrotic syndrome:**
        - Frothy water work
        - Passing red urine
    - **Joint pain**
    - **Skin rash**
    - **Nail change –** Yellow, slow rate of nail growth
    - **Headache**
    - **Hypothyroidism:**
        - Neck swelling
        - Weather preference
        - Weight change

PMH:

- Any medical condition I should be aware of
- Any hospitalization
- Any history of surgery

Drug history:

- Any allergies
- Medication list
- **D-penicillamine therapy**

Family history:

- Family history of similar conditions - **familial disease** has been described
- Any Family history of medical illnesses

Social history:

- What do you do for living?
- How these symptoms affecting you in work and daily living?
- Do you smoke?
- Do you drink alcohol?
- Any financial help or support needed?

Can I examine you?

- Examine legs first – **lymphedema** – bilateral
- **Yellow nails in feet**
    - The **nails are thick**, excessively **curved**, slow growing, leaving bulbous fingertips uncovered and **pale yellow** (or **greenish yellow**)
    - The **cuticles are lost**
    - The **lunulae are absent**
    - **Onycholysis**

- **Chest examination:**
  - **Bronchiectasis**
    - Coarse crackles
    - ? Wheeze
  - **Pleural effusion**
    - There is bilaterally decreased expansion
    - Stony dull percussion notes
    - Absent breath sounds at the bases
    - Associated decreased vocal fremitus

What are your concerns?

- From what you told me and after I examined you, most likely you have a condition called yellow nail syndrome
- It is a rare condition that affects the fingernails and toenails.
- People who develop this condition also have lung breathing problems and problem with the lymphatic channels causing swelling in the lower parts of their body.
- Swelling is caused by a buildup of lymph under the soft tissue of the skin.
- Lymph is a colorless fluid that circulates throughout your body and helps cleanse it.
- Yellow nail syndrome can occur in anyone, but usually occurs in adults over the age of 50
- What we need to do is to arrange some blood tests and imaging to confirm our diagnosis
- We will refer you to group od specialists including chest surgeon, chest doctor, physiotherapist, and occupational therapist for best plan of management
- Is that okay with you?
- Do you have any other concern?

What are your findings?

- On examination of this middle-aged lady, **positive findings** include:

  - On general inspection there is **swelling of the lower limbs**
  - On inspection of the hands, there is **discoloration and deformation of the nails** of the hand and feet, with yellowing and **abnormal curvature** associated with **cuticle loss**

What is the most likely diagnosis based on these findings?

- 'The **triad of yellow nails**, **peripheral oedema** and **respiratory signs** is consistent with a diagnosis of **yellow nail syndrome**.

What are your differential diagnoses?

- Yellow nail syndrome is essentially a **spot diagnosis**, with no true differential diagnoses.
- Therefore, **various alternative differential** diagnoses can be offered, such as:
- **The differential diagnosis of a pleural effusion:**
    1. **Transudates**:
        - CHF
        - Liver failure
        - Renal failure
    2. **Exudates**:
        - Infection (parapneumonic)
        - Malignancy (primary or secondary)
- **The differential diagnosis of lymphoedema:**
    - **Congenital**: **familial lymphoedema**
    - **Acquired**:
        - **Infection** - **filiariasis**
        - **Pelvic mass**
        - **Iatrogenic** - surgical removal of lymphatics
- Alternative diagnoses of **discolored and deformed nails**
    - **Fungal infection** with concomitant but unrelated respiratory pathology

How you will investigate this case?

- Yellow nail syndrome is a **clinical diagnosis**, however a patient presenting with any or all the signs of yellow nail syndrome would receive an extensive investigative work-up.

Basic investigations:

- CBC
- Electrolytes
- LFT
- Inflammatory markers
- TFT

Investigation of pleural effusion

- **Pleural effusion analysis** in yellow nail syndrome classically shows a

1. Clear fluid
2. Lymphocytosis
3. Rich in protein and LDH

Investigation of limb swelling:

- Note that although yellow nail syndrome describes lymphoedema rather than peripheral oedema, it is appropriate to include **investigations relating** to the more common causes of **limb swelling:**

- Urinalysis and urinary protein: creatinine ratio for heavy proteinuria
- Cardiological tests, including a 12-lead **electrocardiogram** and an **echocardiogram**, to **rule out** a primary diagnosis of **heart failure**, which could easily be the **cause of peripheral oedema and pleural effusions**
- **Ultrasound of the abdomen** would provide information on **liver echotexture**, thus **ruling out liver cirrhosis** as a cause of lymphoedema and in the case of lower limb swelling, provide information on any **pelvic masses causing lymphatic obstruction**

Lymphatic investigations.

- Given that specific lymphatic investigations are the remit of **vascular surgery**, 'a referral to a vascular surgeon would be indicated for investigations of primary lymphoedema'

Nail investigations

- Nail **scrapings** **to rule out fungal infection**.

How are you going to treat this case?

- **MDT** – thoracic surgeon, pulmonology
- Management of a pleural effusion

What is the yellow nail syndrome?

- Yellow nail syndrome consists of the **triad of**
    1. **Yellow slow-growing nails**
    2. **Lymphoedema**
    3. **Pleural effusion**.
- It is usually associated with **lymphatic hypoplasia**, ankle **oedema** and several **pulmonary conditions** may occur, such as
    1. **Bronchiectasis**
    2. **Exudative pleural effusion**
    3. **Recurrent pneumonias**
    4. **Sinusitis**

What are the associations of yellow nail syndrome?

- D-penicillamine therapy
- Nephrotic syndrome
- hypothyroidism
- AIDS
- Lymphoedema
- Bronchitis
- Bronchiectasis
- Rhinosinusitis
- Bronchiectasis
- Autoimmune conditions
- Malignancy

Thickened nails and onycholysis
No cuticles or lunulae.
Bulbous uncovered fingertips are suggestive of stunted nail growth
Similar findings would be expected on examination of the **toes**.

Endurance

10-12-2018